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Table of Contents.

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ORIGINAL ARTICLES—

Centenaries of Fifty-One, by Harvey Sutton	461
The Effect of Hyaluronidase on the Absorption of Heparin, by Paul Hagen	471
The Incidence of Retrosternal Fibroplasia in Premature Infants in Sydney, by Eben H. Lipsley	473
Pain in Cardiac Infarction, by J. A. Forbes	475
Tuberculosis Mortality Rates of Native-Born White Australians and Migrants, 1910-1912, 1920-1922, 1932-1934 and 1946-1948, by P. D. Abbott	476

REPORTS OF CASES—

Osteitis Deformans Involving the Jaw, by W. E. Fleming, M.B., B.S., D.D.Sc.	479
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REVIEWS—

A Text-Book of Medical Ophthalmology	480
Massage and Medical Gymnastics	480
A Year Book of Obstetrics and Gynaecology	480
Endocrinology	481
Relief of Pain in Childbirth	481
A Year Book of Paediatrics	481
Porcine Development	481
Fractures, Dislocations and Sprains	481

BOOKS RECEIVED

482

LEADING ARTICLES—

A Literary Jubilee	483
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CURRENT COMMENT—

Neurocirculatory Syndrome	484
The Use of Procaine Amide in Cardiac Arrhythmias	485
Cancer and the Doctor-Patient	485

CENTENARIES OF FIFTY-ONE.

By HARVEY SUTTON,
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In Great Britain and in the Commonwealth this year unusual interest has been taken in the centenary of the Great Exhibition at the Crystal Palace and in the jubilee of the founding of the Australian Commonwealth. It seems appropriate to note once more our own medical centenaries.

The first thing is to decide who should be included in this "who's who in '51". Probably no complete agreement is likely to be reached as to all who ought to be awarded this posthumous fame. The selection by a national committee would almost certainly vary greatly, merely because sources of information are more readily available concerning one's own ancestors. Garrison, for example, never fails to give full value to Americans, just as Castiglioni provides a complete list of Italians; yet both are in general broad-minded and fair in their estimates. English, French and German historians all betray their parochial preferences. That a prophet has no honour in his country apparently applies only during his lifetime. Much will depend on the personal interests of the writer himself.

Recently Garrison and Morton have brought out an invaluable check-list of texts illustrating the history of the medical sciences.

Leslie T. Morton, librarian at Saint Thomas's Hospital Medical School, has revised and written up the bibliography originally compiled by Fielding H. Garrison in 1912 and 1933 and designed by him as a convenient scaffolding for a book on the history of medicine. The idea, it is stated, originally came from Osler, whose own "*Bibliotheca*" is a most helpful and informative basis for the study of medical authors throughout the ages. Garrison and Morton mention

ABSTRACTS FROM MEDICAL LITERATURE—	Page.
Bacteriology and Immunology	486
Hygiene	487
SPECIAL ARTICLES FOR THE CLINICIAN—	
XIV. Haematemesis	488
BRITISH MEDICAL ASSOCIATION NEWS—	
Scientific	490
OUT OF THE PAST	494
POST-GRADUATE WORK—	
The Melbourne Permanent Post-Graduate Committee	495
The Post-Graduate Committee in Medicine in the University of Sydney	495
DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA	495
OBITUARY—	
Magnus John May	496
Myllies Wyamarus Cave	496
Vivian Joseph Mankey	496
Thomas Natal Bolger	496
William Sydney Gleeson	496
HONOURS	496
AUSTRALIAN MEDICAL BOARD PROCEEDINGS	496
NOMINATIONS AND ELECTIONS	496
DIARY FOR THE MONTH	496
MEDICAL APPOINTMENTS: IMPORTANT NOTICE	496
EDITORIAL NOTICES	496

5506 works arranged in chronological order under 55 special aspects of medicine, including all the chief specialties. Almost at a glance one may see how knowledge in the particular subject grew step by step as each successive addition was made to knowledge by each paper. Anyone attempting to depict how knowledge grew from the beginning in his subject cannot do better than study this invaluable reference book. Each paper means a noteworthy advance, and I have therefore used it constantly as a guide in choosing these centenary authors. Altogether it is the most complete and unbiased compilation I know.

"Bailey and Bishop" is another wholly delightful handbook to assist one to a personal knowledge of the individuals whose names are known in every hospital throughout the world. Higginson's syringe, Potain's aspirator, Southeys' tubes and many others are mentioned. We see the portrait of the inventor, a picture of the apparatus, an account of his life and significance, and often some bright and amusing tale of his doings. It is a charming addition to our personal library and in a way pays a well-merited compliment and grateful acknowledgement to those who have made us all more efficient practitioners. Further, the facts this handbook has brought together are often not available elsewhere.

Jessie Dobson's "Anatomical Eponyms" is also useful in this direction of identifying familiar names.

With regard to centenary studies, this cross-sectional method of visualizing medical and scientific activities has obvious limitations, but nevertheless yields at times most interesting findings. It is, of course, a method—random selection—accepted by statisticians. A review of the '51 group shows what useful glimpses one may thus get of the tide of progress in discovery. The emphasis varies strikingly from century to century.

Not much is seen before 1551. For the next hundred years human and comparative anatomy comes to the fore, together with the activities of the (medical) botanist and

naturalist. In 1651 comes a "plum" in the "De Generatione" of Harvey. From this time on a fresh interest in the diseases of women leads up to the widespread development of midwifery in the eighteenth century. Neurology in the early nineteenth century has its supporters, but the most prominent feature is the new advance in biochemistry and biology. Microbiology, too, has laid down its foundations, and the physiologist is "on top of the world". Later in the century come the many investigators who studied the microscopical and biochemical characteristics of parasites of every kind. The viruses and methods of protection against infection are being more and more tackled. Throughout the whole period clinical activities never cease. New diseases, new syndromes and new phases in special fields are continually brought to notice. New techniques are worked out in surgery and in medicine. The late nineteenth century sees endocrines and heredity become subjects of major interest. Thus the cross-sectional method of sampling gives us many examples of the historical trends we know from other sources. The attack is really a triple one. It combines the record of births in that year and of the deaths. Those who die in '51 will be in full activity perhaps twenty years or so before; those who are born in '51 will come to full fruition thirty or forty years later. The third division includes actual events in '51, which will be the product mostly of people born early in the century. We see, then, three great waves of progress in operation and gain an intelligent picture of trends in the development of human knowledge.

What then appears an accumulation of unrelated useless facts mainly of interest to the antiquarian or the historian is shown to illuminate the whole of human progress and to suggest the ways and means by which gains come to us, and possible plans of worthwhile effort in the near future.

While every extension of knowledge only expands the horizon of what we do not know, more power, more control, more encouragement is steadily becoming the possession of the medical profession. The acute infections are, for example, being hustled off the scene. Pestilence, like famine, we are sure can and will be conquered, and with that conquest mankind will truly possess the world on which so many have led so precarious an existence for so many ages.

Claudius Ptolemaeus, A.D. 73 to 151, celebrated astronomer and geographer of Alexandria, was born in Greece (the Thebaid) and died at the age of seventy-eight years. His active period was in the reigns of Hadrian and Antoninus Pius. His mathematical syntaxis was later known as the great syntaxis. The Arabs used the superlative "megistee" and added "al"—"Almagest" (the greatest). It really is a masterpiece; "megale" (syntaxis) means "the great composition". The refraction of light rays was well understood by him.

The "Almagest" had a very great effect on mathematics and established trigonometry, both plane and spherical. The astrolabe was the chief instrument of the mediæval astronomer. With it Ptolemy fairly correctly estimated the distance of the moon from the earth. The world, our world, was the centre of the universe. Around it revolved in seven circles the moon, Mercury, Venus, the sun, Mars, Jupiter, Saturn and the Starry Heavens, all within the *primum mobile*. By ingenious epicycles he could explain and predict the position of the planets. The seven circles Shakespeare alluded to in "King Henry V"—"the seventh heaven of invention". The merits of Ptolemy's geocentric and the Copernican heliocentric scheme (1543) were still being hotly disputed in the time of Christopher Wren. Ptolemy was the first to record the apparently larger size of the moon when it was just above the horizon. He thought it an illusion from an increased idea of distance due to seeing earthly objects in between.

The *Hôtel-Dieu* was founded in A.D. 651 by St. Landry, Bishop of Paris, a nogocomium for the treatment of the sick and a practical outcome of Christian principles. In 1788 it had 1200 beds and far more patients, taking as many as four or more in one bed. Only 486 were single beds. This was overcrowding indeed. Add to this 800 patients in the larger halls on pallets or heaps of straw, and one can

understand the spread of sepsis and the high fatality from operations. When typhus was about, hospital visiting by doctors could be "equivalent to a sentence of death" (Tenon, 1788), and John Howard's investigation did much good; but the cleaning up of these filthy conditions, which overcrowding and understaffing produced, had to wait till Florence Nightingale created modern hospital nursing in 1860.

Trousseau's outstanding work, "The Medical Clinic of the *Hôtel-Dieu*" (1861), demonstrates the excellence of the medical studies and treatment that prevailed in this hospital during the nineteenth century and since.

(Meester) Jan Ypermann (1259 to 1351), of Flanders, a pupil of Lanfranc of Milan, became by his clinical teaching in Paris the founder of French surgery. Later he became the leading surgeon in the Netherlands—he trephined for depressed fracture of the skull and knew how to repair hare-lip. In leprosy he recorded the occurrence of anaesthetic patches and the spread of the disease by sexual intimacy. His "Cyrurgie" was reprinted in 1912.

The University of Glasgow was founded by Bishop Turnbull of that burgh of barony by a Bull of Pope Nicholas V (1451). It was some time before medicine was taught there. Andrew Borde states that he studied there in 1536. As a *studium generale* it was an assemblage of students in the stages of both secondary and tertiary education—that is, both high school and university. Paris, Oxford, Cambridge and Montpellier were similar ecclesiastical foundations. A chancellor ruled and the votes of the masters decided the granting of degrees. Medicine came to be taught as a branch of philosophy ("Physica"). The early graduate had to present and defend theses from ancient authors and take the oath. He was given "a ring, a wreath of laurel and ivy, a book first closed and then opened, the kiss of peace", and greeted as doctor in philosophy and medicine.

In 1451 the Edinburgh Town Council recorded in its minutes (in Latin) the admission of Aitkyne a barber (*barbi tonsor*) to be a burgess. At the request of the Queen (Mary of Gueldres, wife of James II of Scotland) he was granted the freedom of the Guild (of Barbers) for his lifetime without payment except the customary "species et vinum" (spices and wine). He may have been attached to the royal household.

Queen Mary of Gueldres, when her husband died, endowed Trinity Hospital with twelve beds for the permanently disabled, and since its site was taken by the railway last century the funds are still used by the Town Council of Edinburgh for grants to the aged and sick.

Bernard di Rapallo worked out an effective operation for stone in 1451.

Anatomical theatres were opened in 1551 at Paris and Montpellier. Montpellier had led the way in having public dissections in 1366; Paris did not have them till 1478. Padua erected the first anatomical theatre in 1445.

Pierre Belon (1517 to 1564) of Le Mans (Soulterre in Maine), after graduating in medicine and studying botany with Valerius Cordus, spent the years 1546 to 1549 travelling in the Near East as a naturalist. His first book is on Fishes (1551). In this work, though it is based on Aristotle, he gives excellent studies and illustrations of his own, such as the attachment of the embryo cetacean to the mother whale. His well known remarkable study of the skeleton of man and that of a bird side by side shows his insight into comparative anatomy. He visited England on three occasions. In 1564 he was murdered in Paris.

Gabrielle Falloppio (1523 to 1562) of Modena, a pupil of Vesalius, was professor of anatomy at Ferrara at the age of twenty-four years and later (1551) taught anatomy, surgery and botany at Padua. In 1561, the year in which he succeeded his teacher Vesalius as professor of anatomy, appeared his "Observationes anatomical". He gave the best description of the oviducts, which he was the first to call *uteri tuba*. Both Soranus and Vesalius had described them, even though they are now generally known as the Fallopian tubes.

Fallopis was the first to use the words *placenta*, *vagina* and *luteum* (*corpus luteum*). He described the ovary, then known as the female testis. His work on the ear was outstanding and gave the names to several structures, which they still possess—for example, *chorda tympani*, semi-circular canals. He described the trigeminal, auditory and glosso-pharyngeal nerves and the sphenoidal sinus. The *aqueductus Falloppii* is named after him. He wrote on many subjects—mineral waters, “*de morbo Gallico*” (1563—syphilis), surgery, and also on botany, the last-mentioned publication being based on his work in the botanical garden at Padua. Though aged only thirty-nine years when he died, he left an imperishable name.

Conrad Gesner (1516 to 1565), of Zurich, was a most erudite scholar and physician, and perhaps one of the last who might well claim that he knew everything. He brought out a “*Bibliotheca universalis*” of 20 volumes (1545-1549). He was also a truly great naturalist, as is shown in his “*Historia animalium*” in five volumes (1551-1558). He had already written up botany—“*Historia plantarum*”. He was one of the earliest mountain climbers. The “*Historia animalium*” is the starting point and foundation work in modern zoology, for he combined first-rate observation with original and attractive illustrations. Strange to say his best botanical works were not printed till nearly two hundred years after his death (1761-1757).

Hollerius (1551) prescribed spectacles for myopes. Just when spectacles came in is not clear. Nero used an emerald at the gladiatorial combats.

Bartolomeo Maggi (1516 to 1552) of Bologna demonstrated (1551) with experimental proof that to obtain healing of gunshot wounds they should neither be cauterized nor regarded as poisoned and as custom demanded treated with boiling oil. This supported Ambroise Paré's ideas.

The University of Mexico was founded in 1551.

William Turner (1510 to 1568) of London brought out the only original English herbal written in the sixteenth century. It appeared during the years 1551 to 1568 and was fully illustrated. Turner has been called “the father of English botany”. He had already written about birds, the first modern ornithology (in Latin, 1544). He described birds noted by Aristotle and Pliny. In 1538 he had described various plants in his “*Libellus de re herbaria novis*”. Botany was at that time closely linked with medicine and *materia medica*. Turner was evidently a gifted naturalist and had more than once visited the Continent and was a friend of Gesner. To him is given the credit of introducing alfalfa or lucerne into England.

Timothy Bright (1551 to 1615), an English physician, invented shorthand “*Characterie*” (1588). He wrote a treatise on melancholy (1586), which some think was the source of much of Shakespeare's conception of the “mind diseased”. Only one copy of “*Characterie*” is known to exist. Bright had published an abridgement of Foxe's “*Acts and Monuments of the Church*” (1581), was resident physician at Saint Bartholomew's Hospital, and in 1590 gave up medicine for the church. William Harvey took up the same appointment at Saint Bartholomew's Hospital in 1609.

Fortunato Fedeli (1551 to 1637), at Palermo, wrote “*De relationibus medicorum*”, an early treatise on medical jurisprudence (1602). Judging by its frontispiece, many matters were then discussed which still are problems—monsters, foetal formation, hereditary disease, poisoning, and so on.

Francesco Stelluti (1557 to 1651) of Fabriano, Italy, was an original member of the Academy of the Lynx. A poet and naturalist, he was one of the first to use for research the microscope Galileo had just invented. In 1630 he figured the external aspects of the honey bee and of the grain weevil. He was the first to picture the compound eye of the honey bee (as early as 1618).

William Harvey (1578 to 1651) of Folkestone, Kent, studied anatomy under Fabricius at Padua, where he obtained his doctorate in 1602. He brought out “*De generatione animalium*” (1651) at London. This was based mainly on the chick, but includes many original notes on

other animals and is thus one of the earliest essays in comparative embryology. He had carried out dissections of about 50 species of animals, from sponges to mammals, only to lose his manuscripts during the Civil War. His was the first exact description of the air sacs of birds.

Harvey laid stress on the value of the study of the structure of lower animals in throwing light on the biological truths manifest in the human fabric. He criticized anatomists who “confine their researches to the human body alone” and then “when it is dead”. “If, as Aristotle tells us, the immortal Gods were present in the kitchen of Heraclitus, let us not despise the study of the humbler animals.”

In 1651 Harvey demonstrated that warm water injected into the pulmonary artery would return via the pulmonary vein to the heart, thus favouring injection studies. Ent used this in 1657, employing serum of milk as the medium. Ent was a foundation Fellow of the Royal Society and sponsored Harvey's work on generation.

“*De generatione*” in the long search after truth—a search hampered by lack of techniques and instruments which had not yet come into use. The compound microscope, for example, was not yet in use, the only dissections available were done by the unassisted eye or at most with the help of simple hand glasses. Even dissection was looked down upon. The works of Aristotle, Galen et cetera, which he had copied so carefully, and his Paduan teachers, then the leading anatomists of Europe, all gave him ideas, many of which were misleading. At that time and for many years afterwards spontaneous generation of living organisms was generally accepted. Harvey voted for “*omne vivum ex ovo*”.

Redi, in 1668, inspired by Harvey's dictum, disputed the spontaneous origin of life. He urged “*omne vivum ex ovo*”, and showed that visible creatures such as maggots appeared only when flies had access to the material.

In 1766-1776 Needham, who had supported spontaneous generation, was crushed by Spallanzani's studies. Even in Pasteur's time the belief still existed and was again refuted by Pasteur's ingenious experiments.

Harvey upheld the idea of epigenesis, as opposed to preformation and encasement. Epigenesis (“origin over above” in Greek) signifies something new appearing, something that was not there before in that form—the emergence of a structure by differentiation from an original mass of undifferentiated material. Wolff in 1759 made this “theory of generation” quite clear in studies on the formation of the intestine in the chick; but not till 1812 did this conception gain support, thanks to J. F. Meckel's advocacy. Von Baer with his germ layer theories settled the matter (1827). Harvey was indeed 100 to 160 years or more before his time. Even Malpighi, well practised in microscopy as he was (1628 to 1694), thought he saw a minute embryo in an uninjected egg. The growth of, say, a bulb was a process of unfolding of completely formed structures pre-existing. A complete being existed in the egg, and these also had again complete ovaries and eggs in them and so ad infinitum.

When spermatozoa were demonstrated by Leeuwenhoek in 1679, preformation was attached to the male element, and two rival schools sprang up, one supporting the egg (ovists) and the other the spermatists, who held out for the spermatozoa.

The chapter “*De partu*” has been praised as the first original work on midwifery by an Englishman. Harvey was satisfied that the foetal circulation was independent of the mother's blood in the placenta. Bayon has analysed “*De generatione*” and classes it as little if at all inferior to the far better known “*De motu*”. It had its faults and flaws. Harvey's experiments on conception on the deer represent well-planned and accurate observations; but without microscopy the solution eluded him. As an out-and-out admirer of Aristotle he could not free himself from that great naturalist's dicta. It is not, however, till the era of William and John Hunter that better ideas of conception prevailed. John Hunter actually carried out artificial insemination. It was not, indeed, till 1841 that the

complete story of the origin of the spermatozoon had been worked out, and in 1876 the confluence of the two gametes was proved.

Every historical character must be viewed against the background of his time. No one lives in a vacuum. Compared with the works of his contemporaries and their beliefs, Harvey's "De generatione" stands out as a notable contribution to scientific progress.

Nathaniel Highmore (1613 to 1685) of Fordingbridge graduated at Oxford and practised at Sherborne, Dorsetshire. In 1651 he dedicated to Harvey his first work, "Corporis humani disquisitio anatomica", which discusses the circulation. In it is a description of the antrum which led to its being linked with his name—antrum of Highmore, *sinus maxillaris*. However, it was quite well known to older anatomists and figured by Leonardo da Vinci. He described the seminal ducts. The *mediastinum testis* is *corpus Highmorii* or Highmore's body. He also published (1651) "The History of Generation".

Kermes mineral was introduced in 1651 by Johan Rudolph Glauber (1604 to 1688) of Carlsstadt. Glauber, best remembered in "Glauber's salts" (sodium sulphate), knew all the tricks of the alchemist, but was also a first-class chemist. He extracted money from high and low by selling his "secrets". However, Kermes mineral was sold to Louis XIV in 1720. It is composed mainly of antimony trisulphide. Its reddish character suggests certain insects known as kermes, which were among the *materia medica* as well as producing a dye.

A striking effort both for its fine illustrations and its up-to-date study of the fauna and flora of the New World was brought out by the *Accademia dei Lyncei* (*Academy of the Lynx*) in 1651—"Plantarium, animalium, mineralium mexicanorum historia". The Academy of the Lynx, organized by Federigo Cesi, Duke of Aquasparta, was formed in 1609, the first of the great scientific societies. The lynx was renowned for its (supposed) piercing powers of vision, and the society paid much attention to the work of the newly-named microscope. One of their members was Galileo.

Isaac Minnius divided the sterno-mastoid for torticollis by open incision in 1651.

Jean Pecquet (1622 to 1674) of Montpellier, in his "Experimenta nova anatomica", Paris, 1651, announced his discovery of the thoracic duct in dogs and its relation to the lacteals. Aselli, who had previously seen the lacteals, thought they went to the liver.

Olaf Rudbeck (1630 to 1702) of Sweden, trained at Padua, demonstrated the link-up of the intestinal lymphatics with the thoracic duct in 1651. He was able to distinguish them from the lacteals. He published this in 1653. The Dane, T. Bartholinus, reexamined these relations in 1653 and quarrelled with Rudbeck as to priority.

Marco Aurelio Severino (1580 to about 1656) of Calabria, professor of anatomy at Naples, published in 1651 a work on vipers—"Vipera pythia". He was one of the first to dissect a snake. Severino was a contemporary of William Harvey. He was a pioneer in comparative anatomy, or as he called it "Zootomia", and held that it was necessary to round off the study of anranatomy (human anatomy). His book in 1645 was the "Zootomia democritae", Democritus being an opponent of Aristotle, and Severino shared this attitude. The Inquisition was apparently suspicious because of their Aristotelian support. At any rate Severino found it safer to publish the book in Nuremberg. He was a surgeon of note and used freezing mixtures (snow and ice) to produce local anaesthesia for operations (1646), and he was the first to describe the excision of the wrist (1620).

"Frère Jacques"—Jacques de Beaulieu (1651 to 1727)—whom Garrison calls "a strolling incisor"—introduced lateral lithotomy (1697), an operation he perfected by anatomical study. Cheselden, who had written on the "High Operation for Stone" (1723), adopted "Frère Jacques'" method with great success. It is recorded that Cheselden removed a stone from the bladder in fifty-four seconds by the watch.

John Doloeus (1651 to 1707) attributed leucorrhœa to the secretory activity of the lining of the uterus or vagina. This appears in his "Encyclopedie Medicinal", which devoted ten chapters to the diseases of women. Doloeus thought leucorrhœa prevalent in Holland because of the marshy countryside. This was indeed a general belief at the time.

Hendrik van Deventer (1651 to 1724) of The Hague was at first a goldsmith and studied medicine at Groningen, but later practised at The Hague in obstetrics and orthopaedics. His book "Novum lumen" (1701), which was well illustrated, gave the first accurate description of the pelvis and its deformities, and also of the influence of the latter on parturition. In it, too, he illustrates spinal deformities. He considered the "obliquities" of the womb, uterine malpositions, a cause of difficult labour—an idea at least as old as Aetius. Deventer can be looked on as "the father of modern midwifery".

Hejdentryk Overkamp (1651 to 1692) of Holland was one of the first to talk about substances accumulating in the follicles and passing into the circulation.

John Machin, who died in 1751, described *ichthyosis hystrix* (1731-1732), "An Uncommon Case of a Distempered Skin". The Lambert family in whom the condition appeared was followed up with succeeding generations.

Burkhard David Mauchart (1696 to 1751) of Marbach, produced as professor of anatomy and surgery at Tübingen his best work on the eye (1783 to 1786). The alar or check ligaments of the ocular muscles are Mauchart's ligaments.

Julien Offray de la Mettrie (1709 to 1751) of Paris, following the lead given by Descartes in 1664, wrote "L'homme machine" (1748), which was published anonymously at Leyden. The book was ordered by the magistrates to be burnt (La Mettrie took no chances). Religious heresy was even in the eighteenth century a dangerous accusation in many parts of Europe. The whole printing was, so the authorities thought, committed to the flames; but a copy must have slipped through, and the English translation appeared in 1749. The attempt of the author was to prove the materialism of the soul. However, as Garrison points out, the physiologist who thinks only in terms of physics and chemistry has ceased to think physiologically.

The great "Encyclopédie", published in 1751-1772, mainly edited and written by Diderot (1713 to 1784), follows similar lines. At this time a schism had arisen in the ranks of the supporters of preformation, an hypothesis which held the field from Malpighi (1673) till Meckel in 1812 revived Wolff's theory of generation (1759), and von Baer in 1827 completely destroyed this fantastic theory. As noted above Malpighi thought he could see an embryo in an incubated egg (actually the egg was two days old and it was hot weather). A complete being in miniature, so to speak, lay in the egg; it merely had to unfold itself. Being already complete in the egg, it was obvious, the preformationists held, that it had ovaries, and ova in the ovary, and so *ad infinitum*. Eve had in her ovary the forms of all human beings of the future, estimated by one mathematically minded as 27,000,000. It was likened to a series of Chinese boxes one within the other—"emboulement". The supporters of the idea were called "ovists". And then Leeuwenhoek saw minute living forms—animalcules—in the male sperm, and the split took place. La Mettrie and others thought they could see the human form in the head of the spermatozoon and became "spermatists". Wolff attacked the idea of preformation, reverting to the doctrine of epigenesis, the idea of a process of emergence—something developing which was not there before as such—which had been advocated by Harvey and by Aristotle. But Haller and others would not accept this doctrine. Truly, as John Williams recently stated, the "facts" of one generation often become the fantasies of later generations and vice versa.

Abraham Vater (1684 to 1751) of Wittenberg was a student of Ruysh in Amsterdam, professor of anatomy and botany, and later professor of pathology and therapeutics in Wittenberg. He described Vater's ampulla—ampulla

to the bile duct—in 1720, also the tubercle of Vater and the *papilla duodeni* (Santorini's description of this papilla is dated 1724). In 1717 he described the sensory end organs—Vater's corpuscles; they are usually described as Pacinian bodies, though Pacini's account is dated 1840.

Théophile de Bordeu (1722 to 1776), a graduate of Montpellier, held (1751) that secretions peculiar to each of the various organs were essential for vital activities and were each governed by a particular locality of the brain, thus foreshadowing the endocrines and the idea of cerebral localization. Later (1763) he reported on work with spayed animals and eunuchs, discussing the effects of internal secretions of the sex organs passing directly into the blood. He describes striking examples of obesity and extreme shyness (probably of pituitary origin). "Researches on Chronic Diseases. VI. Medicinal Analysis of the Blood" (Paris, 1775) was his best work.

George Cleghorn (1716 to 1789) wrote an account of the diseases epidemic in Minorca (1751). This includes many post-mortem studies and is still read in that island.

John Burton, of York, set out the first statements on the interspinous and intercrystal measurements (1751). He reported in the Royal Society's *Philosophical Transactions* the effective treatment by tying it off of a large cervical polypus filling the vagina. Five days later the shrunken mass dropped off (1750-1755). Burton was the first to assert that puerperal fever was contagious, in his book "An Essay Towards a Complete New System of Midwifery Theoretical and Practical" (1751).

John Fothergill (1712 to 1780), of Carr End, Yorkshire, was a Quaker physician, the leader of the profession in his day. Following Sydenham's example, he wrote his "Observations on the Weather and Diseases of London" (1751-1754), and in the same year assisted Benjamin Franklin to found the Pennsylvania Hospital.

Albrecht von Haller (1708 to 1777) of Berne, the great authority in medicine and physiology of his day, was for seventeen years professor at Göttingen. Here he taught medicine in all its aspects, lecturing on surgery though he had not operated. In 1751 he founded the Royal Society of Science, Göttingen (*Königliche Gesellschaft der Wissenschaften*).

Johann Friedrich Meckel the elder (1724 to 1774) of Wetzlar investigated the nerve supply to the face (1751). He is best known in relation to Meckel's ganglion (sphenopalatine). His son, P. F. T. Meckel, and his grandsons, J. F. (the younger) Meckel and A. A. Meckel, all became famous. Meckel's diverticulum was the discovery of the younger Meckel.

Bartholomew Mosse of Dublin, a public-spirited surgeon, opened (1746) the first lying-in hospital in the then United Kingdom, his own private hospital, and in 1751 began the building of the Rotunda Hospital, Dublin, where he and his successor, Sir Fielding Ould, established sound treatment and instruction in midwifery.

William Smellie (1697 to 1763) of Lanarkshire and London studied midwifery in Paris and set up in London when aged forty-two years. Here he taught obstetrics in his own surgery, using a leather-covered manikin. Among his thousands of pupils were William Hunter (1718 to 1783) and Tobias Smollett, the author of "Roderick Random", who was at first a pupil and later helped to advise on and edit Smellie's text-book. In 1752 came his *magnum opus*—"Treatise on the Theory and Practise of Midwifery". He showed how to measure the diagonal conjugate and stated the criteria of contracted pelvis. He had, in addition to the steel lock, recently introduced the curved and double-curved blades (1751-1753) and set out the first safe rules for the use of the forceps. William Smellie (1752), Fielding Ould (1742) and Charles White (1773) were the pioneers in obstetrics in Britain and Ireland. Smellie was the first to describe Erb's palsy (1768). Erb's paper was published in 1873.

Robert Whytt (1714 to 1766) of Edinburgh, the foremost neurologist of his time, wrote an essay "On the Vital and Other Involuntary Motions of Animals" (1751). This won him his fellowship of the Royal Society at the age of

thirty-eight years. Whytt had a very wide training. As a boy at Kirkcaldy he entered the faculty of arts at Saint Andrews University and graduated in 1730 at the age of sixteen years. Thence he went to Edinburgh for four years under Munro *primus*, Sinclair Rutherford Innes and Plummer. He went on to the Continent to work under Boerhaave, Winslow and Albinus, taking his doctorate in medicine of Rheims in 1736; he returned to Scotland for the doctorate in medicine of Saint Andrews University. His essay showed for the first time that the brain was not essential for reflex action, that in the frog the reflexes for the upper and the lower limbs were in separate parts of the cord, and that only a small section of the cord was needed for a reflex act. He destroyed one of the anterior corpora quadrigemina and showed that the reflex contraction of the pupils to light ceased (Whytt's reflex). The "soul" was then much discussed as to its localization. Whytt held that it was equally distributed throughout the nervous system and originated the movements of muscles (contrary to Haller, with whom he had a thorough discussion). Two excellent clinical studies are to Whytt's credit. In 1764 he wrote "On Nervous Hypochondriac or Hysteric Disorders", and best of all in 1768 "Observations on the Dropsey in the Brain"—a very complete account of tuberculous meningitis. He was professor of the institutes of medicine and also of the practice of medicine (1747 to 1766).

Pennsylvania Hospital was founded in 1751, with Benjamin Franklin (1706 to 1790) of Boston as its principal founder and first president. He wrote and printed at his own press an account of its creation. He was keenly interested in many subjects in science and in medicine, such as treatment by electricity of paralyses (Franklinism, 1757). He flew a kite and got an electric shock; a repetition of this experiment by a European professor ended fatally. Especially interesting in his invention of bifocal lenses (1784). He was a great supporter of inoculation against smallpox.

Lucas Johann Boér (1751 to 1835) was a leading Vienna obstetrician, one of the first perhaps to emphasize that pregnancy is a normal physiological state. He noted incomplete rupture of the uterus and used incision of the cervix—vaginal Cesarean section. His outstanding work is "Treatment and Researches in Midwifery Conditions" (1791 to 1806—two volumes).

William Roxburgh (1751 to 1815), surgeon and botanist, superintendent of the Calcutta Botanic Gardens (1793 to 1813), wrote "Plants of the Coast of Coromandel" and "Memoir on a New Species of Sweetenia (Mahogany)", comparing the powers of its bark with those of Peruvian bark, for which it is proposed as a succedaneum (substitute).

John James Laforest Audubon (1785 to 1851) produced a great modern atlas of the birds of America (1827 to 1838). This was followed by the text "Ornithological Biographs" (1831-1839).

Konrad Johann Martin Langenbeck (1776 to 1851) of Horneburg was professor of surgery and anatomy in Würzburg and later at Göttingen. He wrote a "Handbook of Anatomy" (1831-1847). Langenbeck's nerve is the posterior supraclavicular nerve. He was surgeon-general of the Hanoverian army (1814). He worked out iridocleisis for artificial pupil and his speed as an operator was outstanding. Langenbeck is said to have performed an amputation of the shoulder while a colleague standing by was taking a pinch of snuff. In the days before general anaesthesia the surgeon sought to combine speed with skill. He had indeed to be bloody, bold and resolute.

Antoine Lembert (1802 to 1851) described (1826) how to ensure that serous surface should unite with serous surface by means of his well known ingenious suture for enterorrhaphy—Lembert's suture.

Jean Guillaume Auguste Lugol (1786 to 1851) of Montauban graduated and practised in Paris. In his lectures on pathology at the Hôpital Saint-Louis he recorded that cases of "scrofula naturally ended in pulmonary consumption". Scrofula is a somewhat vague term. It included tuberculous glands of the neck, hip and knee,

spinal tuberculosis, and certain eye conditions (phlyctenule). No doubt deficiency of vitamin D was typically associated. Its prominence was enhanced by the annual touching by the King combined with the gift of a gold touchpiece; the "Angel for scrofula the King's Evil". Some said "What the Sovereign could not cure the half-sovereign did". From Henry II to Anne this ritual was regularly followed, but George I would have nothing to do with it. Charles II broke all records during his reign, for he had a very warm heart for the poor. In twenty years he touched 92,000 persons. Lugol advocated fresh air, exercise, cold bathing and iodine. The last-mentioned is administered in various ways. For oral use he employed a watery solution of iodine (5%) and potassium iodide (10%). Nowadays as scrofula has ceased, Lugol's solution is given in thyroid conditions as set out by Plummer of the Mayo Clinic (1924).

Francois Victor Mérat de Vaumartoise (1780 to 1851) of Paris discussed colic, commonly called the colic of painters, plumbers and plumbum (1803), giving an excellent description of lead as an industrial hazard and its effects.

Samuel George Morton (1799 to 1851) of Philadelphia trained at Edinburgh and taught anatomy. His chief fame is in the fine atlases he published on American (1839) and Egyptian skulls and (1834) his studies of pulmonary consumption, which the then recent industrialization had forced into prominence. He was also a pioneer in the systematic studies of fossils in America (1834). His opinions on the fertility of the hybrids of diverse human races roused the theologians to fierce attacks. He is said to have had a collection of over 1000 skulls.

Christian Friedrich Nasse (1778 to 1851), Berlin, drew attention in 1820 to the freedom of females from the manifestations of haemophilia, though through the females the condition was transmitted—Nasse's law.

Lorenz Oken (1779 to 1851) of Swabia (Bohlsberg) was a biologist of some note and a leading light of "Naturphilosophie", of which he wrote in 1802 "Foundations of Naturphilosophie". Oken was professor of natural history at Jena and Göttingen, and also taught in Basle, Munich and Zurich. Immanuel Kant of Königsberg, in his "Critique of Pure Reason" (1771) discussed the place of purpose of ends. While acknowledging that Nature shows us nothing in the way of purpose, yet we can understand an organism only if we look on it as though it was produced under the guidance of thought for that end. Kant held that a hidden basic principle of Nature unites the mechanical and teleological. Many today regard teleology as incompatible with the scientific method and scientific progress. The study of purpose of ends is to them fatal to unbiased study of phenomena. Yet constantly and almost instinctively the embryologist, the anatomist, the physiologist and the biochemist use language which implies this basic principle of purpose. Goethe (1795 to 1807) and Oken followed up these thoughts into comparative morphology and into the study of segmentation as the plan or archetype of the animal body including the skull. The vertebral theory of the skull collapsed when Rathke discovered the part played by the gill arches, for example, in the formation of the mandible and the ear, and Huxley insisted on the decisive function of embryology in settling these developmental processes. As he said, "There is no greater tragedy in Nature than the destruction of a beautiful theory by an ugly fact".

Huxley clearly distinguished between homology (agreement), similar relation to the general type, and analogy, a functional similarity quite apart from its origin. The back legs of a horse have their main joint (hock) analogous to the knee, but it undoubtedly is homologous to our ankle. All knees bend back. The horse's stifle joint is homologous to our knee.

Oken, in "Die Zeugung" ("Generation"—1805) foreshadowed the cell theory. He definitely stated that all organic beings originate from and are made up of vesicles or cells, and that these form the *Urschleim* (later called protoplasm) whence all organisms are built up. In his study of Infusoria he gives a clear idea of their structure.

He was indeed an embryologist of note, founded the biological journal *Isis* (1816 to 1848), and first organized an annual meeting of scientists (1821), setting a fashion which is now universal. The British Association for the Advancement of Science held its first meeting in 1831.

Jones Quain (1795 to 1851) of London published his "Elements of Descriptive and Practical Anatomy" in 1828; its eleventh edition appeared in 1929. How many doctors living today cut their teeth, anatomically speaking, on "Quain", "Gray" and "Ellis" plus "Cunningham"?

John Kearny Rodgers (1793 to 1851) of New York City was the first American surgeon to tie the left subclavian artery (within the scaleni) for aneurysm; however, the patient did not survive (1845). In 1827 he wired an ununited fracture of the ulna with good results.

Thomas Addison (1793 to 1860) of Longbenton, North Cumberland, with Sir William Withey Gull (1816 to 1890) of Colchester, described in *Guy's Hospital Reports* (1851, Volume LI, page 52) vitiligoidea or xanthelasma (xanthoma).

Friedreich Arnold (1803 to 1890) of Landau studied at Heidelberg and was professor of anatomy at Zurich, Freiberg, Tübingen and Heidelberg. He completed his "Handbook of Anatomy" in 1851. Several structures have been linked with his name: Arnold's ganglion (otic ganglion, fifth nerve); Arnold's auricular nerve (a branch from the root ganglion of the vagus); Arnold's recurrent nerve (a link of the first division of the fifth to the fourth cranial nerve); Arnold's innominate canal (in the sphenoid carries the lesser superficial petrosal nerve).

E. Bascomme wrote the "History of Epidemic Pestilences" (1851). In it he tells how in A.D. 664 two kings of Erin called a council both of churchmen and of citizens because of "a general dearth". They all agreed that a general fast should be observed (easy enough in a famine). A motion was put that prayers should be offered up beseeching God to remove by pestilence "the burthensome multitudes of the inferior people". This was passed, and a suggested amendment asking Divine help to increase the produce of the land to satisfy the needs of the people was turned down. History relates that the pestilence came quickly and almost wiped out the passers of the decision of the council.

Claude Bernard (1813 to 1878) of Saint Julien, working on the cervical sympathetic of the rabbit (1851), saw on dividing the nerve a rise in temperature and pronounced dilatation of the vessels of the ear, the first demonstration of the vasomotor mechanism. He was then the holder of a chair at the Sorbonne in Paris.

Secondo Berruti of Turin founded a laboratory for experimental physiology (1851) where Moleschott did excellent work.

Theodor Maximilian Bilharz (1823 to 1862) of Sigmaringen found in 1851 a new nematode, *Heterophyes heterophyes*, and also a new tapeworm, *Hymenolepis nana*. Neither of these had the pathological interest of the *Schistosoma hematobium*, the well known Bilharzia he saw in 1850. This work was done in the post-mortem room of the Kasr-el-Aini hospital in Cairo when he was working with Griesinger.

Sir Benjamin Collins Brodie of Winterslow, Wiltshire (1783 to 1862), was a student at Saint George's Hospital and later full surgeon, Fellow and President of the Royal Society. He was also an original Fellow of the Royal College of Surgeons in 1843 (president, 1844). In his 1851 edition of his important work "On the Diseases of Joints", he noted the bursa around the tendons of the semimembranosus and the gastrocnemius. Brodie's abscess is a solitary abscess of bone (often the tibia). His name is also given to serocystic disease of the breast.

Charles Edouard Brown-Séquard (1817 to 1894) described the well-known syndrome Brown-Séquard's paralysis, in which damage to one lateral half of the spinal cord gives rise to motor paralysis of the same side and to loss of sensation on the other.

John Murray Carnochan (1817 to 1887) of Savannah, Georgia, a bold surgeon of the mid-nineteenth century, tied

the femoral artery (1851). He is recorded as having excised the ulna, the radius and the *os calcis*. He also excised the fifth nerve (second branch) for neuralgia in 1858, the first operation of the kind.

Johann Ludwig Casper (1796 to 1864), the German leader in legal medicine, wrote on judicial post-mortem examinations (1851-1853). His writings, "Practical Hand-book on Legal Medicine" (1851-1858) and others, made him the outstanding authority of his day.

Charles Marie Edouard Chassaignac (1805 to 1879) of Nantes, a leading surgeon in Paris, wrote a series of studies on anatomy and surgical pathology (1838 to 1851). His name is best known in connexion with the *tuberculum caroticum* on the sixth cervical vertebra—Chassaignac's tubercle. The cellular interspace between the *pectoralis major* and the mammary gland is called Chassaignac's space or bursa. In his "Practical Treatise on Suppuration and Surgical Drainage" he showed the way to use rubber tubes in the drainage of abscesses (1859).

Jacob Augustus Lockhart Clarke (1817 to 1880) of Pimlico, neurologist and physician to the National Hospital for the Paralysed and Epileptic, London, wrote papers in *Philosophic Transactions of the Royal Society* (1851 to 1853). He is best known in connexion with Clarke's column in the spinal cord (1851) and Clarke's cells. With Hughlings Jackson he described syringomyelia (1867).

Clot Bey-Antoine Bartholomy Clot (1793 to 1868) of Marseilles graduated in Marseilles and Montpellier and then departed for Egypt in 1823. Here for twenty-seven years he acted as chief surgeon both to the ruler of Egypt, the Viceroy Mehemet Ali, and to his army. In 1827 he established a school for military medical officers at Abu Zabal, through which 420 qualified in the next ten years. Dissection was a difficulty. At first he used the dog as the corpse, but it had to be the dog of a Jew or a Christian. Later, corpses of Christians and of Negro slaves were permitted to be used. Special permission had to be obtained from the theologians for a post-mortem examination to be held. At first everything had to be translated into Arabic, but this of course shut off the student from text-books and other sources of modern medical literature. French finally was adopted, and French and Italians formed the teaching staff. The test came with the cholera epidemic of 1831. In 1832 he took 12 of his best students to Paris, where they successfully passed their doctorate test. Clot Bey himself wrote a number of medical text-books in Arabic. In 1837 he transferred the school to the old Palace Kaar el Aini in Cairo, where Ibn el Aini had built a fortress (Kaar = castle) and residence in 1466. This took 300 students, fed, boarded and clothed them, and provided them with pocket money—all at the expense of the State (1837). Here they received a five years' course. Veterinary, pharmacy and midwifery schools were soon organized. When Mohamed Ali died in 1848, Abbas I took his place as Khedive. Clot Bey returned to France. The medical school became the scene of international conflict; French, Egyptian, German and Italian teachers followed in turn and intrigue was rife, so that Said Pasha in 1855 closed the school and sent the students into the army. But his army lacked military doctors, and Clot Bey was brought back the next year (1856). He made great efforts, but his health gave way and he returned to France (1858). He died in Marseilles in 1868 at the age of seventy-three years. Among his clinical papers he wrote on *elephantiasis scroti*, the vesical calculi and lithotomy, cholera epidemics and the Hejaz pilgrimage, plague in Egypt (1848), ophthalmia, trichiasis, entropion and cataract in Egypt. Perhaps the most important endeavour for which Clot Bey did splendid work was the Sanitary Congress in Paris in 1851, just a century ago, the real start of international health cooperation.

Marchese Alfonso Corti (1822 to 1888) of Sardinia, an histologist who worked in several centres (Vienna, Berlin, Utrecht and Turin), was associated with Hyrtl, Müller, Kolliker, Gegenbaur and others. His paper on the ear in mammals (1851) is best known in regard to the organ of Corti in the cochlea and the rods of Corti.

Charles-Victor Daremberg (1817 to 1872) of Dijon, one of our best medical historians, translated Oribasius (1851-

1876). His "History of the Medical Sciences" (1870) is still read.

Charles Darwin (1809 to 1882) published in 1851 his first independent scientific monograph on the *Cirripedia* (barnacles). At first attracted by medicine and then by the church, Darwin had finally taken up botany under Henslow at Cambridge. He studied geology under Sedgwick (both Henslow and Sedgwick were clergymen). Henson obtained for him a job as (unpaid) naturalist of the *Beagle*, with strictly limited space and almost no time for work. His scientific results obtained during his voyage in the *Beagle*, 1831, were brought out (1839-1840) in the well-known *Journal of Researches*. J. D. Hooker took the journal with him on the *Erebus* and *Terror* to the Antarctic (1839-1843) and later confirmed Darwin's botanical data collected in the Galapagos. Darwin suffered from ill-health and was rather confined to his house. Here one room was devoted to the tank for his barnacles, on which every few hours he made detailed records. His wife tells how she was on a visit to a relation with one of her boys. She found him one day wandering all over the house, poking his nose into every room, apparently looking for something. His mother asked the boy what he was looking for. His reply was to ask: "Where does Uncle keep his barnacles?"

Josef Dietl of Cracow (1804 to 1878) was a member of the New Vienna school who doubted that any treatment could hope to cure disease. Dietl asserted: "As long as medicine is art it will not be science. As long as there are successful physicians there will be no scientific physicians"—a helpless and hopeless attitude (1851). His name is remembered only for the critical fever, vomiting and pains in "floating" kidney when a ureteral kink develops (Dietl's crisis), described in 1864 in his work on "Wandering Kidneys".

Friedrich Theodor von Frerichs (1819 to 1885) of Aurich wrote on Bright's disease (1851). At that time he was probably the leading authority on internal medicine and did more than anyone to develop clinical teaching along scientific lines.

Otto Funke (1828 to 1879) of Heidelberg wrote papers on the venous blood in the spleen (1851-1852), in which the discovery of haemoglobin was announced.

Pierre Nicholas Gerdy (1797 to 1856) of Loches was anatomist, pathologist and surgeon in Paris. Gerdy's ligament (*ligamentum suspensorium axillæ*), Gerdy's fontanelle (sagittal fontanelle near the obelion) and Gerdy's tubercle (on the lateral tuberosity of the tibia for the ilio-tibial band) are all recorded in his "Practical Surgical Practice" (1851).

Horace Green (1802 to 1866) of Vermont, the first to take up laryngology in America, was the first to draw attention to cystic and malignant growths in the larynx (1851). He had written an early text-book (1846) on rhinolaryngology.

William Griffith, an Anglo-Indian surgeon and a botanist of note, brought out his "Icones plantarum Asiaticorum" (1847-1851).

Samuel David Gross (1805 to 1884) of Easton, Pennsylvania, was the leading surgeon of his day in the United States of America and professor first in Kentucky (1840 to 1856) and then in Philadelphia (1856 to 1882). A versatile writer, he wrote a history of surgery in Kentucky (1851) and later of American surgery (1876). His was "the milk-white flower of a stainless life" (Garrison).

J. G. Hebenstreit worked on Greek medical terms (1851).

Heintz was the first to isolate bilirubin (1851). Gmelin's nitric acid test for bile pigment dates back to 1826.

Hermann von Helmholtz (1821 to 1894) of Potsdam, and of German, English and French ancestry, was both a famous physician and physicist. His invention of the ophthalmoscope (1851) made the study of vision truly scientific.

Wilhelm Hofmeister (1824 to 1877), a leading biologist in Germany, wrote his epoch-making work on the botany of the Cryptograms (1851). The word "hidden marriage" suggested that the flowers and seeds were concealed.

Hofmeister in the fern showed the alternation of generations, sexual and asexual, spermatozoids and ova (archegonia) alternating with spores which through the prothallus developed the spermatozoids and archegonia. He followed the methods of fertilization in the pines and in flowering plants; on this plants have been arranged into main groups—thallophyta *et cetera*.

Thomas Henry Huxley (1825 to 1895) of Ealing received the fellowship and gold medal of the Royal Society (1851) for his research into marine zoology, much of which was carried out while he was a surgeon of the Royal Navy during the cruise of Her Majesty's Ship *Rattlesnake* (1846-1850), during which he frequently visited Sydney.

Kiwisch of Prague brought out his "Text-book of Obstetrics" in 1851. His name is associated with the invention of special uterine sounds at the same time as those of Huguet and Simpson (1843).

Joseph Leidy (1823 to 1891) of Philadelphia, anatomist and a capable naturalist and parasitologist, made in 1851 the first attempt to transplant malignant tumours.

Justus von Liebig (1803 to 1873) of Darmstadt pointed out (1851) that the blood gases were probably in loose combination with some substance (later identified as haemoglobin). Liebig, one of the first great organic chemists, provided a classification of foodstuffs and was closely linked to activities in Britain.

Carl Friedreich Ludwig (1816 to 1895) of Hesse, professor of anatomy at Marburg and also of physiology at Zurich, demonstrated the nerve supply of the submaxillary glands (1851). Later on he worked in Vienna, and finally at his own Physiological Institute in Leipzig, completing a lifetime of nearly forty years of scientific study and teaching.

Sir James McGrigor (1771 to 1858) of Strathspey studied at Marischal College, Aberdeen and Edinburgh. He retired in 1851 at the end of fifty-seven years' service (1793 to 1851) in the army. For the last thirty-five years of this period he was director-general of the medical and sanitary services of the army. Just as Larrey had been Napoleon's right-hand man, so McGrigor had been the right-hand man of Napoleon's conqueror, the Duke of Wellington.

Gustav Adolf Michaelis (1798 to 1848) of Kiel published his classic work on pelvic deformities "Das enge Becken" (1851). He named the rhachitic type of pelvis. His most famous patient was Frau Adametz, on whom he performed her fourth successful Cæsarean section (1836).

Hugo von Mohl (1805 to 1872) of Stuttgart and Tübingen wrote (1846-1851) on the content of the vegetable cell, and gave the name protoplasm to the semisolid material just under the cell wall, distinguishing it from the watery sap in the middle of the cell. Purkinje had invented this name for embryonic ground substance in 1839. Schultze established its modern use (1863) and showed its identity in all living cells, while Flemming (1882) gave the description of its intimate structure.

Jacob Moleschott (1822 to 1893) of Holland was a keen student of metabolism and nutrition. He opposed Liebig and was a leading materialist. His "Physiologie des Stoffwechsels in Pflanzen und Thieren" (1851) emphasized the series of chemical changes in the body taken as a whole. In 1850 he had done excellent work on food analysis and adulteration. He was also an enthusiastic Darwinian. From 1861 to 1879 he was in charge of the laboratory founded at Turin by Berruti in 1851.

Heinrich Müller (1820 to 1864) of Leipzig, in his paper on the histology of the retina (1851), first described the visual purple or rhodopsin. This substance bleached by light is closely linked with vision at low illuminations (scotopic). Its regeneration is retarded in vitamin A deficiency, a fact that attracted great attention in the air force during the recent war.

August Nélaton (1807 to 1873) of Paris (*Hôpital Saint-Louis*) was the first to describe unmistakably the pelvic haematocele. Bernutz in 1848 had considered any collection of blood in the pelvis as due to regurgitation of menstrual fluid. Nélaton spoke of retrouterine, circumuterine and periuterine haematocele. McClintock gave the name

pelvic haematocele, and in later years the relation to a ruptured ectopic gestation came to be appreciated. Nélaton also helped forward ovariotomy. He is probably best remembered in regard to Nélaton's line. In 1851 he wrote "Of the Influence of Position in Surgical Illnesses".

Sir James Paget (1814 to 1899) of Great Yarmouth, England, trained and taught at Saint Bartholomew's Hospital. He made his name as a surgical pathologist, and his first work of note was his "Lectures on Tumours" (1851). His best work is his "Surgical Pathology" (1863). His name is still retained in Paget's disease (*osteitis deformans*) (1877) and Paget's disease of the nipple preceding cancer (1874). With Owen he formed the selection committee that sent out G. B. Halford to inaugurate the Melbourne Medical School in 1863.

Charles-Gabriel Pravaz (1791 to 1853), a French surgeon, introduced the hypodermic syringe (1851) and published an account of it in 1853. Alexander Wood of Edinburgh (1817 to 1884) invented independently (1853) an effective syringe on the plan of the sting of a bee, especially for giving morphine to relieve pain. Pravaz had earlier (1841) introduced the electrocautery (applied to the cure of aneurysms, 1853).

The name of Nikolai Ivanovich Pirogoff (1810 to 1881) is the greatest in Russian military surgery. He served in the Caucasus and the Crimea. He is remembered chiefly by his amputation (1854), but his best work is probably his anatomical atlas (1852-1854), the first to employ frozen sections. He was one of the first to use ether as an anaesthetic (1847). His "Clinical Surgery" appeared in 1851-1854.

Franz Pruner (1808 to 1882) of Oberpfalz (Pruner Bey) studied at Munich and Paris and when a professor at the military school of medicine, Abuzabel, near Cairo, carried out many epidemiological studies and ethnological researches. In 1851 appeared his paper "The World Plague Cholera and the Policy of Nature", which followed his monograph on "Bubonic Plague" (1839) and his work on "Diseases of the Orient and Their Nosology" (1847). He did pioneer work in the classification of races by their hair, judging by texture and cross-section (1872).

Ernst Reissner (1824 to 1878) of Riga, in a work published at Dorpat (1851), described the *membrana vestibularis* of the cochlea, Reissner's membrane.

William W. Reid (1799 to 1866) of Rochester, New York, in 1851 worked out the way of reducing dislocations purely by manipulation without any use of weights or pulleys (cases of dislocation of the femur on the *dorsum ilii*).

Felix Adolphe Richard (1822 to 1872) of Vitz-our-Seine, a Parisian surgeon, described in 1851 the trumpets of the uterus. Richard's fringes is the group of fimbriae of the ostium of the Fallopian tube. He also named the accessory openings of the tube "pavillons accessoires".

Max Johann Sigismund Schulze (1825 to 1874) of Freiburg was an anatomist and histologist and described the segmentation of the frog's egg (1863). In 1851 he concluded his studies of marine zoology (Turbellaria). Some of his best work was on the nerve endings of sensation. He introduced chromic acid solution and osmic acid staining. He was the first to use a heated object stand.

Karl Theodor Ernst von Siebold (1804 to 1885) of Wurzburg in 1851 named the trematode found by Bilharz in Cairo *Distomum heterophyes*; it is now known as *Heteropyle heterophyes*. Siebold was then at Breslau. When he was at Freiburg (1845 to 1850) Bilharz was his best pupil in zoology and comparative anatomy. He infected dogs with *Tania echinococcus* and classified hookworm among the Strongylidae.

Joseph Toynbee (1815 to 1866) of Hockington, Lincolnshire, otologist of London and lecturer at Saint Mary's Hospital, wrote on the structure of the *membrana tympani* in the human ear (1851) and on its functions (1852). The *tensor tympani* (so named by Albinus) is sometimes termed Toynbee's muscle.

Armand Trousseau (1801 to 1867) of Tours, professor at Paris and physician of the *Hôtel-Dieu*, was a pioneer in intubation (1851) and had performed the first tracheotomy

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(1831). He is best known for his work on infantile tetany. He wrote important treatises on therapeutics (1836), clinical medicine (1861), tuberculous and chronic laryngitis (1837), glycosuria (1865) and the medical clinic of the *Hôtel-Dieu* (1862).

Verany described varieties of octopods. He noted (1851) that the long arm might drop off if touched; the other arms had to be torn away.

Andrea Verga (1811 to 1895) of Milan, professor of clinical psychiatry, described in 1851 the space between the *corpus callosum* and the fornix body—Verga's ventricle.

Augustus Volney Waller (1816 to 1870) demonstrated in 1851 the well-known phenomenon of degeneration in the distal part of the nerve axons after a nerve had been divided—a most valuable technique in the experimental study of the nervous system (Wallerian degeneration). The degeneration is simultaneous in action. Regrowth of the axon may follow at the rate of roughly four millimetres a day.

Walter Hayle Walshe (1812 to 1892) of University College Hospital, London, reported the presystolic element in the murmur in mitral stenosis in his work "A Practical Treatise on the Diseases of the Heart and the Great Vessels" (1851).

Alexander William Williamson (1824 to 1904) of Wandsworth, London, entered at Heidelberg (1840) as a medical student, but changed to chemistry under Gmelin and later under Liebig at Gressen. At Paris, where he went after graduation, he studied mathematics under Comte and became professor of practical chemistry (1850 to 1887) at University College. In 1851 he brought out papers on molecular mobility, showing that oxidized substances, whether organic or inorganic, might be regarded as replacement of the hydrogen atoms in the type molecule of water.

George Wilson wrote "The Life of Cavendish" in 1851.

One of the first meetings, if not the first meeting on the world scale, was the International Congress on Statistics at Brussels in 1851, which was followed the next year by the International Congress on Hygiene and Demography held in the same city. Adolphe Quetelet (1796 to 1874) had placed Belgium in the forefront by his monographs "*Sur l'homme*" (1836) and on his theory of probabilities applied to the moral and social sciences, published at Brussels.

In 1851 the University of Minnesota was founded at Minneapolis; the University of Pavia was reopened; the Georgetown University (District of Columbia) founded its medical faculty; the *Wiener medicinische Wochenschrift* was founded; the College or Commonalty of the Faculty of Physic, London, of 1518, became by Act of Parliament, 1851, the Royal College of Physicians.

The Great Exhibition of 1851, sponsored by the Prince Consort Prince Albert and housed in great glass pavilions at the Crystal Palace, had by its remarkable publicity extensive effects on our ways of living. Professor W. A. Osborne considered that it introduced a world-wide consumption of sweets. Australia is said nowadays to lead the world in sugar consumption. What influence this "sweet tooth" may have had on the increase of dental caries and on diabetes is not quite clear, but it may be said to be under suspicion.

Robert Abbe (1851 to 1928) of New York City used catgut rings in intestinal anastomosis (1892).

Karl Martin Paul Albrecht (1851 to 1894) of Hamburg studied in Jena, Berlin, Vienna and Kiel, and finally taught anatomy in Brussels. He wrote on a new bone at the base of the skull (1883). This is the basioccipital and the basisphenoid (Albrecht's bone).

Jacques Arsène d'Arsonval (1851 to 1940) of Paris introduced high-frequency currents into electrotherapy. In 1892 appeared his paper on *la voltaisation sinusoidale*.

Francis Maitland Balfour (1851 to 1882) of Edinburgh and Cambridge worked together with Michael Foster and brought out a "Text-book on Embryology" (1874). His next research was on the cartilaginous fishes (Elasmobranchs), including the shark and the ray, especially their embryology, and was carried out at Naples. Returning to

Cambridge as lecturer on animal morphology, he brought out his magnificent "Comparative Embryology" (1880-1881), an outstanding review of all previous work and a masterly summary of all that was then known on the development of living forms. His master work may be regarded as the foundation of the modern study of embryology. In July, 1882, he was accidentally killed while mountain climbing, soon after he had been made a professor at Cambridge.

Charles Lucien Beurmann (1851 to 1923) of Paris, with Gougerot first described sporotrichosis.

Martin Willem Beyerinck (1851 to 1931) of Amsterdam found the living fluid from tobacco plants, showing that tobacco mosaic disease was still contagious even after passage through a bacterial filter. These were the first studies of virus infections.

Jacques Bertillon (1851 to 1914), a statistician, presented a thorough investigation of the depopulation in France (1880-1911) and of the effect of a falling birthrate.

Émile Bourquelet (1851 to 1921) studied the soluble ferments in fungi and the synthesis of glucosides (1913 to 1920), while with Bertrand in 1896 he discovered tyrosinase.

James Cantlie (1851 to 1926) of Dufftown, Banffshire, was a graduate of the University of Aberdeen and later worked under Mitchell Bruce at Charing Cross Hospital, London. Here he qualified for his fellowship of the Royal College of Surgeons and went on the staff. In 1883, as one of a band of 12 young doctors, he was sent out to assist in a serious epidemic of cholera in Egypt. After completing the first-aid handbook for the Saint John Ambulance Association, which Peter Shepherd had begun, he went off to the Zululand front and had much to do with the creation of sanitary sections. His interest in the Saint John Ambulance Association and in the Red Cross Society was lifelong and invaluable. In 1887 he joined up with Patrick Manson in Hong Kong, where they founded a first-class medical school which still flourishes. Here he gained a great experience of surgery and of tropical diseases. One of his pupils was Sun Yat Sen, later to become the first president of the Republic of China. In 1897 Cantlie returned to London. He specialized in liver diseases and studied the technique of the diagnosis and operative treatment of liver abscess. In 1914 he gave his experience in the detection of the outlines of solid and hollow viscera in the chest and abdomen by the combined use of tuning fork and stethoscope. He gave the first description of *dermatitis plantaris bullosa*. In 1897 he helped to found *The Journal of Tropical Medicine and Hygiene* and the corresponding society. He was on the staff of the Seamen's Hospital at the Albert Docks, and took an active part in the foundation and teaching of the great school of tropical medicine in London, now incorporated in the London School of Hygiene.

Cantlie was indeed a man of parts. Knight of the Order of the Bath, he preached at Saint Martin's in Trafalgar Square on Hospital Sunday. He thought one should always walk at full speed and at full stride; indeed, his whole life was like that. Its most exciting episode was when Sun Yat Sen had been kidnapped by the Chinese Legation for official disposal in China. A note dropped out of a window reached Cantlie, who by prompt action secured official backing and Sun's release.

Charles Chamberland (1851 to 1898) of Paris, with Pasteur and Roux, studied the cause of anthrax (1880), and for the first time used an attenuated bacterial virus for treatment. The Pasteur-Chamberland filter served a valuable part in separating off the filter-passers or viruses. It has been much in use in water purification, and is mainly made up of a candle of unglazed porcelain.

Hans Chiari (1851 to 1926) wrote a "History of Pathological Anatomy (Human)" in Puschmann's handbook, which is considered the best modern account of the development of pathology (1903). In the same year he wrote on diseases of the aorta of syphilitic origin. He also made an important study of gastric syphilis in 1891.

André Chantemesse (1851 to 1919) experimented with inoculations to give protection against typhoid fever (1888).

Sir Arthur Henry Downes (1851 to 1938) of London, and T. P. Blunt, in "Researches on the Effect of Light on Bacteria and Other Organisms" (*Proceedings of the Royal Society of London*, 1877), were the first to show that sun-light was bactericidal. They thought this effect was due to oxidation.

Emil Pierre Marie van Ermengem (1851 to 1932), a Belgian bacteriologist, isolated the *Bacillus botulinus* from a case of food poisoning (ham).

Raimondo Feletti (1851 to 1928) with Grassi studied the development of the malarial parasite in birds (1891), confirming the findings of Laveran.

Sir Peter Johnston Freyer (1851 to 1920) introduced his method of prostatectomy (1900). His success greatly popularized the operation.

Ernst Fuchs (1851 to 1930) of Vienna was ophthalmologist at Liège and Vienna. In 1885 he noted depressions on the anterior surface next to the pupillary edge of the iris (stomata of Fuchs and angle of Fuchs). His monographs relating to the eye—uveal sarcoma, blindness, sympathetic ophthalmia, test types—are excellent, but his fame rests on his great text-book (1889), a bulky volume which has gone through many editions. Fuchs's optic atrophy (peripheral atrophy of the optic nerve) was reported in 1885. Fuchs's spur is seen where the pigment epithelium invades the stroma midway in the *sphincter iridis*.

Sebastiano Giovannini (1851 to 1920), Vienna, in 1887 described a rare infection of the hair by a fungus (Giovannini's disease).

Markus Hajek (1851 to 1941), professor of laryngology at Vienna, wrote a classic work on the accessory nasal sinuses and their inflammatory disorders (1899). He discussed fully their pathology and the treatment indicated.

George Huntington (1851 to 1916) of Philadelphia published his striking account of the hereditary type of chronic chorea arising in middle life and ending in insanity (1872). An early description prior to this had been unearthed in the correspondence of Robley Dunglison (1798 to 1869) of Philadelphia. The case was sent in by Charles Oscar Waters (1816 to 1892) and published in Dunglison's "Practice of Medicine" (1842).

Paul Kraske (1851 to 1930) introduced the sacral route for a complete excision of the rectum for carcinoma in 1891.

Moritz Loewit (1851 to 1918) of Prague, professor of pathology at Innsbruck, published studies on physiology and pathology of the blood and lymph; erythroblasts have been called Loewit's cells.

Vittorio Marchi (1851 to 1908) of Novellara, Italy, studied in Modena and became anatomical assistant there; later at Pavia with Golgi. He later became director of hospitals at Florence and later at Modena. The antero-lateral descending tract of the spinal cord is often called Marchi's tract (also Lowenthal's tract). His paper on degeneration following extirpation (total or partial) of the cerebellum appeared in 1887.

Samuel John Meltzer (1851 to 1921) of Boston has to his credit many excursions into experimental medicine and physiology. In 1880-1883 he worked with Kronecker on the mechanism of deglutition and in 1905-1906 with Auer on the effect of magnesium salts on tetanus; in 1909 he and Auer worked out a satisfactory technique for intratracheal insufflation—"continuous respiration without respiratory movements". In 1917 he reported a non-surgical method of drainage from the gall-bladder of bile via the duodenum, and discussed the law of contrary innervation as a pathogenic factor in diseases of the bile ducts and gall-bladder.

Julius Leopold Pagel (1851 to 1912), a Berlin physician and a medical historian of note, translated Mondeville and Mesue. His first history of medicine came out in 1897. In 1900 he issued a dictionary of medical biography, and in 1901-1906 an encyclopedic medical history; he also produced a medical chronology in 1908. His small history was reprinted and edited by Sudhoff. The encyclopaedia

was planned by Puschmann and brought out in collaboration with Neuburger—a very fine reference work. Ernest Playfair of London translated the earlier volumes into English.

Arnold Pick (1851 to 1924) of Gross-Meseritsch studied at Vienna and later in Berlin and Prague. He became director of Dobrzau Asylum and later psychiatrist at the University of Prague. Pick's bundle, described in 1889, is an anomalous bundle of nerve fibres in the medulla connected with the pyramidal tract. He drew attention to the development of aphasia arising from circumscribed atrophy of the brain in presenile dementia (Pick's disease).

Gustav Pommer (1851 to 1935) published his valuable researches on osteomalacia and rickets (1885).

Frank Thomas Paul (1851 to 1941) of Pentney, Norfolk, trained at Guy's Hospital and became the first resident medical officer of the Liverpool Royal Infirmary. Later he was full surgeon, after a preliminary period on the staff of the Stanley Hospital and the Southern Hospital. He invented Paul's glass tube and rubber tubing used in abdominal surgery everywhere, and worked out the detailed technique of colectomy. He had a wonderful record in abdominal surgery and was a first-class histopathologist. Discussing his skill, Moynihan stated that "he did with his hands what Pavlova did with her feet, only Paul's work was much more useful" (quoted from "Bailey and Bishop"). With Caton he tried (1893) to treat acromegaly by decompression of the skull.

Walter Reed (1851 to 1902) of Harrisonburg, Virginia, was the son of a Methodist clergyman, Lemuel Sutton Reed, and of Pharaba White of North Carolina. He studied at the University of Virginia, entering at the age of sixteen years. Though some thought him too young, he was third on the list in the final examinations. Working at Bellevue Medical College, New York, he gained his degree of doctor of medicine. The chances of security and of scientific investigations led him to enter the army medical service. His first appointment was in Arizona. The usual experience, he was told, was that after going west to Arizona one later went east to a lunatic asylum. With his recently married bride he "trekked" to San Francisco, a twenty-two days' journey, and with special intervals of study he remained quartered mainly in the west in garrison life from 1876 to 1893, during which period he had been in fifteen different posts. His chance came in 1891, when he took out a complete course in pathology and bacteriology at the Johns Hopkins Hospital, Baltimore. His keenness earned him the post at the Military Medical Academy at Washington as professor of bacteriology and the rank of major.

When the Spanish-American war broke out in 1898 Reed took charge of a commission to study the typhus epidemic raging among the troops. The spread of infection was held to be a question of personal contact and the infected belongings of the sick. They also thought drinking water might play a part. Sanarelli had announced that he had found the organism responsible for yellow fever in 1897, but Reed and Carroll proved in 1899 that the so-called *Bacillus icteroides* was a variety of the swine cholera bacillus and its association was accidental. In 1900 Reed went out to Havana to look into a severe epidemic of yellow fever. With him were Carroll, bacteriologist, Lazear, entomologist, and Agramonte, pathologist. Thirty-five patients had been isolated at Pinar el Rio and 11 died. None of the sisters were infected, nor was the laundryman who handled the dirty clothes. Strangest of all, a prisoner in the nearby gaol developed the disease. This suggested insect transmission. Carlos Finlay, a locally born oculist of Irish descent, who had studied mosquitoes for twenty years, held that *Stegomyia* was the go-between. They realized that human volunteers were needed. At first the mosquito tests gave negative results. This was puzzling, as no one knew that it took eleven or twelve days for the mosquito to be able to hand on its infection. Lazear apparently hit on this and deliberately allowed himself to be bitten by a mosquito infected from a patient some time before. He duly developed the disease and paid the supreme penalty seven days later (September 25, 1900). He, by

arrangement, had his action regarded as accidental to avoid possible difficulties with the life assurance company. Carroll was also infected but recovered, and other volunteers were tested on the new lines and mosquito transmission by *Stegomyia (Aedes aegypti)* was completely proved. John R. Kissinger, the first soldier volunteer, received a decoration. Finlay's hypothesis was thus established, and the way was opened for the control of one of mankind's deadliest enemies. Further tests demonstrated that sleepers in the sick-room or the bed or those handling clothing soiled by the sick got on perfectly well as long as mosquitoes were not admitted. Bad ventilation signified nothing, the infected mosquito signified everything. Volunteer experiments gave approximately four days as the human incubation period. Many control experiments were carried out, and Reed announced the discovery in February, 1901, at the Pan-American Congress at Havana, in his paper "The Etiology of Yellow Fever"—a fitting opening to the twentieth century. Yellow fever in 1793 killed over 41,000 persons in New Orleans and 10,000 in Philadelphia. In the nineteenth century close on half a million had died in America. Since Reed's outstanding research, the demonstration by Gorgas and years later the immunization method of Sawyer, yellow fever has become open to control and serious epidemics in civilized countries are no longer likely. In 1902 Major Reed died after an appendicitis operation and was buried in the great Arlington cemetery at Washington.

Mikolaj Reichmann (1851 to 1918) of Warsaw described in 1882 the disease named after him, Reichmann's disease—gastroesophageal reflux. A pupil of Billroth, he investigated gastric cancer.

Robert William Reid (1851 to 1939) of Auchindoir, Aberdeen, was assistant to Struthers in Aberdeen and later became demonstrator of anatomy at Saint Thomas's Hospital. Later he became professor of anatomy at the University of Aberdeen (1889 to 1925). His paper on the relation of the principal fissures and convolutions of the cerebrum to the outer surface of the scalp appeared in *The Lancet* in 1884. The anthropometric base line on the skull is Reid's base line.

Ottmar Rosenbach (1851 to 1907) published his treatise on "Diseases of the Heart and Their Treatment" (1893 to 1897). In 1876 he brought in his bile test, and in 1880 stated the law deciding the site in the vocal cords of immobilization in complete and in incomplete paralysis of the recurrent laryngeal nerve.

William Stirling (1851 to 1932) won a prize for his graduation thesis "On the Summation of Electric Stimuli to the Skin" (1875), published in the *Arbeiten aus der Physiologischen Anstalt zu Leipzig*. Stirling was a pupil of the great Ludwig and became himself a great teacher. He wrote a treatise on physiology (1888). In 1902 he brought out a most interesting historical study, "Some Apostles of Physiology", magnificently illustrated, and in 1904-1905 he wrote in *The Medical Chronicle*, Manchester, a review of the activities of the school of Salerno.

Johnson Symington (1851 to 1924) of Taunton graduated at Edinburgh in 1877. He became demonstrator of anatomy under William Turner and in 1893 professor of anatomy at Belfast. He was made a Fellow of the Royal Society in 1903. His chief interest was in topographical anatomy and the anatomy of the child. In 1889 he wrote on the rectum and anus. The fibromuscular mass in the perineum between the coccyx and the anus is called Symington's ano-coccygeal body. Symington visited Australia for the meeting of the British Association for the Advancement of Science in 1914.

Victor Clarence Vaughan (1851 to 1929) of Mount Airy, Missouri, was professor of hygiene and director of the hygienic laboratory, University of Michigan, from 1887 to 1909. He studied poisonous proteins (he wrote with Novy "Ptomaines and Leucomaines" in 1864), also bacterial toxins and the cleavage products of proteins. In 1896 he found the poison-producing organism in ice-cream and cheese. In 1898, with Reed and Shakespeare, he studied typhoid fever in war camps and showed transmission by flies. In 1907 he studied anaphylatoxins. In 1916 he

founded *The Journal of Laboratory and Clinical Medicine*. One of his most colourful experiences was with Gorgas in Cuba during the Spanish-American War (1898), when during a severe outbreak of yellow fever at Siboney they decided to burn down the entire village (and its house mosquitoes).

THE EFFECT OF HYALURONIDASE ON THE ABSORPTION OF HEPARIN.

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THE current technique of evaluating hyaluronidase activity in mammalian tissue by the dermal dye spreading reaction is not altogether satisfactory, the margin of the area is not clearly defined and the effect of local variations in skin tension cannot always be assessed. In order to devise some simple method whereby one could determine whether hyaluronidase was or was not active in mammalian tissues under varying conditions, this investigation on the influence of hyaluronidase on the rate of absorption of heparin was undertaken. Moreover, as the route of administration of heparin for clinical purposes is at present a matter of considerable interest, the effects were compared of heparin injected intravenously, intramuscularly and subcutaneously with and without hyaluronidase.

Five adult rabbits were used.

Seeing that the main aim was to find out whether hyaluronidase did or did not significantly influence the rate of absorption of heparin, the dose of hyaluronidase was what was considered to be excessive—two Schering units (equal to 200 Benger units). The hyaluronidase used was of commercial origin; it was mixed with the heparin in the syringe immediately prior to injection.

The doses of heparin used were 200 units, 500 units, 1250 units and 3000 units. A separate series of experiments was performed at each dose level.

Design of Experiment.

A Latin square pattern was used, the first rabbit receiving heparin intravenously, the next heparin hypodermically, the next heparin intramuscularly, the next heparin with hyaluronidase hypodermically, and the fifth heparin with hyaluronidase intramuscularly. The rabbits were transposed each day for five days, so that by the fifth day each rabbit had received each of the five types of injection. The mean of the results is shown in Table I and Figure I.

Coagulation time was used as a measure of blood heparin levels. Only freely running venous blood was used, being obtained from the rabbits' ear veins, and thread formation in capillary tubes was taken as the endpoint. This has been found to give reproducible results in rabbits (Pichotka and Reichel, 1950).

With a dose of 200 to 500 units of heparin given intravenously, the coagulation time was doubled during the first hour—but returned to the preinjection level within one and a half hours. Intramuscular and subcutaneous injections produced no significant effect.

With 1250 units injected intravenously, there was a prolongation of coagulation time, at first to well over eighty minutes and returning to normal in about three hours. Intramuscular and hypodermic injections gave variable results, usually about twice or three times the initial coagulation time and lasting two or three hours.

With 3000 units given by all routes, definite alterations in the coagulation time develop; they can be seen quite well in Figure I.

It can be seen that in adequate doses heparin is more rapidly and completely absorbed in the presence of hyaluronidase, although the effect is never as great or as rapid as when equal doses are given by vein.

TABLE I.

Injection.	Coagulation Time in Minutes immediately before and at Various Intervals after Injection. ¹										
	Before.	Half an Hour.	One Hour.	One and a Half Hours.	Two Hours.	Two and a Half Hours.	Three Hours.	Three and a Half Hours.	Four Hours.	Four and a Half Hours.	Five Hours.
Heparin (intravenous) ..	8	80+	80+	80+	80+	77	71	55	18	10	6
Heparin (subcutaneous) ..	3	7	23	35	39	41	41	37	34	24	11
Heparin (intramuscular) ..	2	8	10	28	37	38	28	25	19	14	10
Heparin with hyaluronidase (subcutaneous) ..	2	12	41	68	73	79	70	58	53	42	23
Heparin with hyaluronidase (intramuscular) ..	2	13	49	74	78	73	64	54	49	42	27

¹ The figures are the means of the five combinations of the Latin square pattern.

For clinical use heparin given intramuscularly or subcutaneously with hyaluronidase should be expected to have a quicker and more pronounced effect on coagulation time than when given without hyaluronidase.

some more convenient method of administration. Coagulation time as a measure of heparin absorption was a much simpler means of determining hyaluronidase activity than, for example, the estimation of dye levels in the blood, following the injection of dyes together with hyaluronidase.

It is surprising that heparin can be used for this purpose in view of McLean's report that heparin inhibits testicular hyaluronidase activity in the streptococcal decapsulator test (McClean, 1942). It is also known that heparin

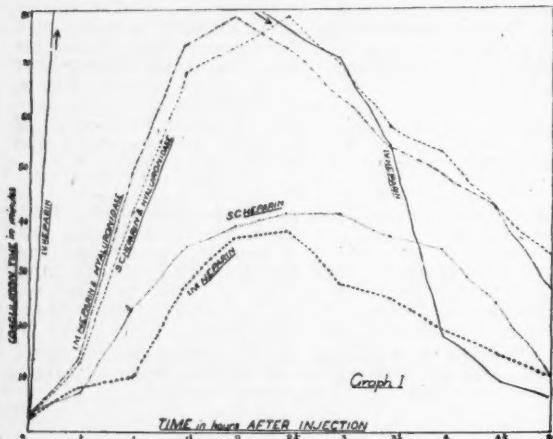


FIGURE I.

More interesting, however, is the possibility of the use of heparin in assessing the ability of certain substances to antagonize hyaluronidase activity in mammalian tissues, and this is illustrated below in the case of "Antistine".

TABLE II.

Injection.	Coagulation Time in Minutes at Half-Hourly Intervals after Subcutaneous Injection. ¹		
	Half an Hour.	One Hour.	One and a Half Hours.
Heparin and saline ..	6	9	9
Heparin and saline with "Antistine" ..	8	14	13
Heparin and hyaluronidase ..	14	42	56
Heparin and hyaluronidase with "Antistine" ..	16	43	48

¹ Mean of results of the four combinations of the Latin square (0.3 unit of hyaluronidase).

Heparin was used as an indicator of hyaluronidase activity mainly because it was the simplest substance to begin with and because it was thought that it might give some information of immediate clinical value. Heparin at present when administered clinically has to be given by vein every four hours, and a means is being sought to find

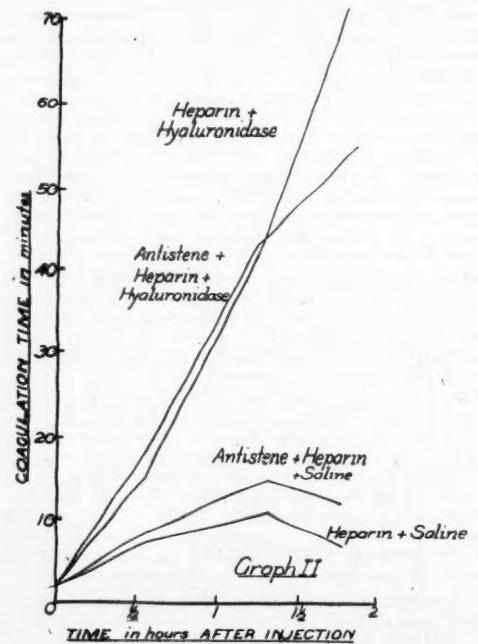


FIGURE II.

inhibits hyaluronidase hydrolysis of hyaluronic acid (Meyer, 1947); this inhibition was probably a substrate competition, hyaluronidase activity being present when high hyaluronidase/heparin ratio existed. Presumably the enzyme became attached preferentially to the sulphated mucopolysaccharide (heparin) rendering it inactive against the non-sulphated hyaluronic acid. Whether the heparin was inactivated in such circumstances was not known.

To find out whether this was so, heparin and hyaluronidase were incubated together; 2000 units of heparin were incubated for one hour with 10, 3.0, 1.0, 0.3, 0.1 and 0.03 Schering units of hyaluronidase. Subsequent injection of these solutions into rabbits' veins completely prevented clotting in blood taken from the rabbits half an hour later; this showed that heparin activity was not affected by the hyaluronidase in these concentrations.

When 5000 units of heparin were incubated with 10, 3-0, 1-0, 0-3, 0-1 and 0-03 Schering units and then injected subcutaneously, they had no more effect on the coagulation time than heparin injected subcutaneously without hyaluronidase; this indicated that the hyaluronidase had been

Five
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27Coagula-
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TABLE III.

Injection.	Coagulation Time in Minutes at Half-Hourly Intervals after Subcutaneous Injection. ¹		
	Half an Hour.	One Hour.	One and a Half Hours.
Heparin and saline	9	11	15
Heparin and saline with "Antistine"	13	13	15
Heparin and hyaluronidase	11	45	65
Heparin and hyaluronidase with "Antistine"	10	12	15

¹ Mean of results of the four combinations of Latin square (0-15 unit of hyaluronidase).

inactivated. It is inferred that in the first experiments described, in which hyaluronidase was mixed with the heparin in the syringe immediately prior to injection, there had not been time for inactivation of all the hyaluronidase.

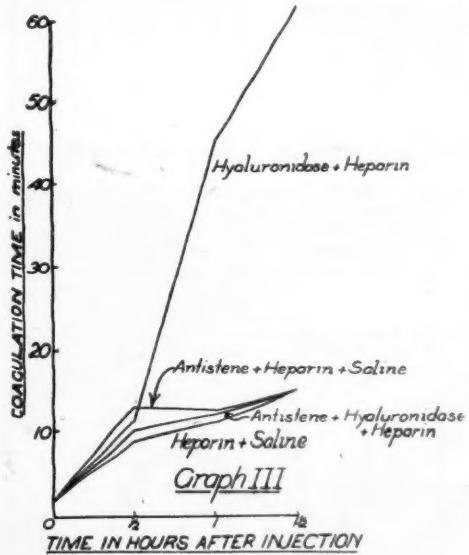


FIGURE III.

Influence of the Antihistaminic "Antistine" on Hyaluronidase In Vivo.

Mayer (Mayer and Cull, 1947) has suggested that antihistamines inhibit the activity of hyaluronidase as measured by the dermal dye spreading technique. Moynihan and Wilson (1949) found no in-vitro inhibition of testicular hyaluronidase by "Benadryl" and other antihistamines.

For the purpose of investigating this four rabbits were used.

Two received 5000 units of heparin with saline subcutaneously. Two received 5000 units of heparin with 0-3 unit of hyaluronidase in saline subcutaneously.

One of the first pair and one of the second pair had received 50 milligrammes of "Antistine" intramuscularly half an hour before.

The technique was varied so that half the hyaluronidase, in 0-5 millilitre of saline, was injected first, the syringe was then disconnected, the needle being left in position, and then the heparin and the rest of the hyaluronidase in one millilitre of saline were injected through the same needle. The coagulation time of the blood was followed only for one and a half to two hours.

A Latin square pattern was followed, each rabbit receiving each combination, so that the experiment was repeated four times. Results are shown in Table II and Figure II.

The "Antistine" did not in any way influence the coagulation time. The difference between the effect of heparin with and without hyaluronidase was more pronounced than in the previous experiments.

The whole experiment was repeated with half the quantity of hyaluronidase, and in this case the "Antistine" reduced the coagulation time curve following administration of heparin and hyaluronidase to the same level as that following heparin administration alone. The results are shown in Table III and Figure III.

Summary.

1. Hyaluronidase increases the rate and degree of absorption of subcutaneously or intramuscularly injected heparin. Its effect is greater if some of the hyaluronidase is injected separately at the site before the injection of the heparin.

2. The inhibition of hyaluronidase activity by heparin has been confirmed.

3. Hyaluronidase does not inactivate heparin.

4. "Antistine" in a dose of 50 milligrammes inhibits the activity of 0-15 Schering unit of hyaluronidase, but fails to inhibit 0-3 unit under the conditions of the experiment.

5. It is suggested that this technique is of value for determining hyaluronidase activity and the activity of hyaluronidase inhibitors in mammals.

6. Hyaluronidase should prove clinically useful in heparin administration.

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THE INCIDENCE OF RETROLENtal FIBROPLASIA IN PREMATURE INFANTS IN SYDNEY.

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INTEREST in retrorenal fibroplasia has been stimulated recently in the United States of America by reports that an increasing proportion of premature infants were developing the lesion. Kinsey and Zacharias (1949) found that at the Boston Lying-in Hospital, in the group whose birth weight ranged from three to four pounds, the incidence of retrorenal fibroplasia in 1938-1942 was one case in 106 premature infants (0-95%), and this rose sharply to 33 in 162 premature infants (20-2%) in the 1943-1947 period.

Hepner and associates (1950) reported that no patients who subsequently developed retrorenal fibroplasia were born at the Chicago Lying-in Hospital before 1937, but the incidence of retrorenal fibroplasia from 1937 to the end of

1945 was 68% of all survivors weighing less than 1600 grammes (three and a half pounds) at birth; from 1946 to the end of 1948 the incidence was 30.4% in the same weight group.

The only published data which give an indication of the incidence of the condition in an Australian city are reported by Campbell (1951) for Melbourne. In presenting clinical evidence that intensive oxygen therapy may have been a cause of retrobulbar fibroplasia, she gives the figures for groups of infants treated with high-oxygen and moderate-oxygen therapy for the years 1948-1950, the infants being of thirty-two weeks' gestation or less (approximately three and a half pounds). In the high-oxygen group Campbell found 23 cases in 123 infants (18.7%) and in the moderate-oxygen group four cases in 58 infants—a total of 27 cases in 181 infants (6.7%).

In Sydney, Gregg (1950) reported having seen several cases in prematurely born infants. As no information was available regarding the incidence of the condition in Sydney, a survey was undertaken in association with the Institute of Child Health to determine the incidence in premature infants.

The Sydney Survey.

Method.

The present study was made by sending questionnaires to parents of surviving infants who weighed three pounds or less at birth and who were born at three Sydney hospitals or who were admitted to the Tresillian Homes. The period covered was from June, 1944, to June, 1949. When ocular defects were reported in the answer to the questionnaire, details of the lesion were obtained by writing to the ophthalmologist in charge of the case, or in doubtful cases the child was examined by a specialist. The children were all between twelve months and five years of age at the time of the survey. It was considered that a serious eye defect was unlikely to have passed unnoticed by the mother if the child was over twelve months of age.

Circulars were dispatched to the parents or guardians of 146 children. Answers were received in the case of 86 children. Over a similar period Isbister and Armstrong (1951) examined a further series of 11 premature infants weighing three pounds or less at birth at a fourth hospital and reported no cases of retrobulbar fibroplasia. Their results have been included in the totals given in Table I.

In the analysis of the following series of infants one case of detached retina has been included under the term "retrobulbar fibroplasia" although no actual fibroplastic membrane was evident. This is justified by the fact that Owens and Owens (1949), who were able to watch the progressive development of the disease in nine cases, reported that "retinal oedema and detached retina which billowed forward in folds" preceded the full development of the lesion and that the disease often became arrested at this earlier stage. In the remaining four cases the typical fibroplastic membrane was evident.

Results.

In Table I is shown the incidence of eye lesions in the group.

Retrobulbar fibroplasia was present in five of 97 cases studied. In two additional cases serious eye defects were present, but in one of these it was not possible to see beyond the lenses because of dense cataracts, and it is probable that in the other case the condition was unrelated to the disease under discussion.

In Table II is shown the distribution of birth weights in the group, together with the birth weights of children with retrobulbar fibroplasia and those with other serious eye defects. It should be noted that three out of the six children weighing less than two pounds developed the lesion. In no case did the condition appear in an infant weighing over two pounds nine ounces.

Discussion.

The most complete study of the incidence of the condition has been carried out by Kinsey and Zacharias (1949), who investigated the occurrence in a number of hospitals in the

United States of America and in one hospital in England. In Table III are set out the results found by these authors for the birth-weight group under discussion (three pounds or less), together with the results of the Sydney survey.

TABLE I.
Incidence of Eye Lesions in Premature Infants (Weighing Three Pounds or Less at Birth).

Surviving Premature Infants.	Serious Eye Defects Absent.	Retrobulbar Fibroplasia (Including Retinal Detachment).	Other Serious Eye Defects (Excluding Retrobulbar Fibroplasia).
97	90	5	2

A comparison of the results indicates that retrobulbar fibroplasia did not occur as frequently in Sydney premature infants as in those born in some cities in the United States of America over a somewhat similar period of time.

TABLE II.
Distribution of Birth Weights of Premature Infants Born 1944 to 1949 in Sydney in a Group Studied.

Birth Weight.	Number of Children.	Cases of Retrobulbar Fibroplasia.	Other Serious Eye Conditions.
1 lb. 12 ozs. to 2 lb. 0 oz.	6	3	0
2 lb. 0 oz. to 2 lb. 3 ozs.	6	0	0
2 lb. 3 ozs. to 2 lb. 6 ozs.	9	1	0
2 lb. 6 ozs. to 2 lb. 9 ozs.	11	1	1
2 lb. 9 ozs. to 2 lb. 12 ozs.	19	0	0
2 lb. 12 ozs. to 3 lb. 0 oz.	35	0	1
Total	86	5	2

It is not possible to compare the Sydney results with figures for Melbourne reported by Campbell (1951), because her group included infants of birth weight approximately three and a half pounds or less, whereas the present survey covered the birth-weight group three pounds or less.

TABLE III.
Incidence of Retrobulbar Fibroplasia Occurring in Infants with Birth Weight of Three Pounds and Less Reported by Various Authors.

Location.	Period.	Number of Premature Infants.	Cases of Retrobulbar Fibroplasia.
Boston Lying-in Hospital	1938-1942	44	9
	1943-1947	38	10
Providence	1941-1947	30	7
Baltimore	1935-1944	23	0
	1945-1947	33	4
Hartford, Connecticut ..	1948	7	4
New York	1939-1946	65	5
Cincinnati	1943-1947	22	2
Birmingham, England	1945	21	0
Sydney	1944-1949	97	5

The fact that three out of six infants less than two pounds in weight developed retrobulbar fibroplasia indicates that this condition is a major hazard of this birth-weight group.

Summary.

A survey was made of the incidence of retrobulbar fibroplasia in a group of surviving infants of birth weight three pounds or less, born in Sydney from 1945 to 1949. Ninety-

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seven infants were included in the study, of whom five developed retrosternal fibroplasia. There were six infants in the group weighing less than two pounds, of whom three developed the condition.

Acknowledgements.

Professor Lorimer Dods, Director of the Institute of Child Health, Sydney, and Dr. Norman McAlister Gregg have given advice and assistance in the making of this survey.

I am grateful to Dr. Kathleen Winning, and to the honorary medical staffs and medical superintendents of the Royal Hospital for Women, Paddington, the Women's Hospital, Crown Street, the King George V Memorial Hospital for Mothers and Babies and the Tresillian Homes, who have made the records of these hospitals available.

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PAIN IN CARDIAC INFARCTION.

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THE reports on 167 consecutive cases of cardiac infarction discovered at post-mortem examination in the Department of Morbid Anatomy, Royal Melbourne Hospital, from April 12, 1949, have been examined and individually correlated with the clinical histories.

The histories were those taken as a routine measure in the hospital by resident medical officers, and the post-mortem examinations were performed by three people using a standard method of examination.

That the histories were not taken with special reference to the cardio-vascular system does not detract from this report, not only because their composition was supervised for statistical purposes, but also because they form a good index of the type of history generally elicited by medical men in their approach to a general medical or surgical problem. The histories were examined particularly for an account of the pain which might have been associated with the occurrence of the infarct. In many the examining doctor made specific comment as to the likelihood that the pain might be cardiac in origin. In some histories in the series, in which the occurrence of vague pain was noted, comments such as "this does not appear to be cardiac in origin" were made.

Two groups have been segregated. The term "recent" is applied to those infarcts in which fibrosis was not apparent on macroscopic examination, their maximum age being about three weeks. Circumscribed scars are classified as old infarcts. This macroscopic classification was confirmed by microscopic examination in many cases.

Of the subjects, 65% were males with an average age of about sixty-five years, the males being on the average about two years younger than the females at the time of death.

Thirty-nine per centum of the subjects had had recent infarcts only, whilst in 26% the infarcts were healed, and some of these patients died of a cause not primarily related to the heart. In the remaining 35% of cases, old and

recent infarcts were recognizable together in the same heart.

The cases are again subdivided into those in which a history of pain in the chest, often similar to the classical descriptions of cardiac pain, is given, those in which the pain is vague, perhaps occurring only in the upper part of the abdomen or back and of a type not usually considered as being of cardiac origin, and lastly, those in which no pain is described. In some cases in the last group there was evidence of specific questioning in regard to cardiac pain. That the descriptions of pain in those cases in which "vague pain" was noted were indeed unconvincing is reflected in the fact that the diagnosis of cardiac infarction was usually not made.

Table I shows the occurrence of pain in these cases. Patients admitted to hospital in coma and unable to give a coherent history were excluded primarily from the series.

TABLE I.

Type of Pain.	Percentage of Total Number.
Pain of cardiac origin (including angina of effort) ..	55
Vague pain of doubtful origin ..	12
No pain described ..	35

Table II illustrates the occurrence of pain in relation to recent and old infarcts, and shows that the figures are not entirely prejudiced by patients who have had old infarcts and have also bad memories. Of the patients with old infarcts 44% gave accounts of pain recognizable as being of cardiac origin, in comparison with 55% of patients with recent infarcts at the time of death.

TABLE II.

Type of Infarct.	History of Pain.	Percentage of Each Group.
Old (102) ..	No pain. Vague pain. Cardiac pain.	53 3 44
Recent (123) ..	No pain. Vague pain. Cardiac pain.	30 15 55

It is not remarkable that the history of cardiac pain is more frequently recorded in cases of recent infarction, for in some of these the pain described is not severe and would be soon forgotten. This would also occur in those cases in which vague pain not recognizable as being of cardiac origin was noted.

Analysis of Cases in Which Cardiac Pain was Present.

Old Infarcts.

Of the 45 subjects with old infarcts associated with an old history of cardiac pain, 23 gave a history of angina of effort. The onset of this history of angina was at times associated with some acute illness, often described by the patient as "flu". At times the onset of angina was heralded by an attack of pain recognizable as being due to cardiac infarction.

The others of this group described pain of the type possibly associated with cardiac infarction.

Recent Infarcts.

Six patients of the 68 with recent infarcts who had pain in the chest and were subsequently shown to have recent infarcts at post-mortem examination described anginal pain

occurring recently, and no other pain; but obviously members of this group would have little opportunity for exercise, unlike those of the group with healed infarcts in which the incidence of angina of effort is higher.

The 62 subjects with recent infarction who had the pain of cardiac infarction (not related to exercise) included some in whom previous infarctions had occurred and who developed angina of effort subsequent to this. About 8% of this group had suffered from angina of effort for some time prior to the recent infarct without an old infarct being found.

It was observed that cardiac pain, excluding angina of effort, occurred in all cases (19) in which thrombotic occlusion of a coronary artery was observed, except in two subjects who were admitted to hospital in coma, no history being obtained.

Pain in Relation to Diagnosis.

The proportion of patients with cardiac infarction who do not complain of pain appears to be greater than is commonly believed. This is confirmed by—and contributes to—the fact that the majority of those cases in which pain was absent or vague were not diagnosed as cardiac infarction; indeed some subjects in whom old cardiac infarcts were present had not consulted a doctor. Some of these patients gave an account of an acute disease which they called "influenza" immediately preceding the onset of angina of effort; others apparently interpreted their symptoms in terms of current infectious disease.

In some cases of recent infarction an electrocardiogram contained no significant changes, although in one or two cases the presence of an infarct which had not caused pain was recognized. On the other hand, in some of these cases of recent painless infarction the condition was assumed to be pulmonary, the patient who had had previously unrecognized hypertension now presenting with a blood pressure ostensibly within normal limits and with signs and symptoms of early pneumonia; consequently no electrocardiogram was made.

The occurrence of cardiac infarction in most cases was characterized by sudden circulatory failure with low blood pressure for that individual, not always with clinically recognizable venous congestion and usually with pulmonary basal crepitations—a condition at times indistinguishable from shock. In other cases, suddenly developing congestive cardiac failure caused the patient to consult the doctor.

Accounts of repeated recent fainting attacks apparently due to cerebral anoxia were not infrequent, and occasionally suddenly developing coma comparable with a cerebro-vascular accident was the mode of presentation.

In an odd case, an intractable attack of asthma disguised the symptoms.

Summary.

The occurrence of pain in association with cardiac infarction is observed in 167 cases of cardiac infarction by relating individual histories and post-mortem reports.

The series indicates that the proportion of cases of painless cardiac infarction is greater than is commonly believed—namely 35%, with a further 12% in which pain was vague and not recognizable as being of cardiac origin.

All subjects with thrombotic occlusion of a coronary artery gave a history of related cardiac pain, but these comprised a total of 19 subjects only.

The occurrence of cardiac infarction a short time prior to death was usually accompanied by sudden circulatory failure often indistinguishable from shock, often by suddenly developing congestive cardiac failure, at times by repeated fainting attacks and occasionally by coma comparable to that of a cerebro-vascular accident. On the other hand, in some cases old infarcts were found in subjects who had given histories of angina of effort dating from an acute painless illness, at times called influenza, for which they had not consulted a doctor, and in others the occurrence of an infarct had apparently been associated with symptoms mild enough to be considered unimportant by the patient.

Acknowledgement.

I wish to thank the medical staff of the Royal Melbourne Hospital for permission to use hospital records for this investigation.

TUBERCULOSIS MORTALITY RATES OF NATIVE-BORN WHITE AUSTRALIANS AND MIGRANTS, 1910-1912, 1920-1922, 1932-1934 AND 1946-1948.

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THE current migration programme has created some interest in the relative incidence of tuberculosis occurring in migrants and in native-born white Australians. It is therefore relevant to examine the difference in mortality rates from tuberculosis in these two groups and to note how this has varied.

Although this examination will not reveal any differentials in the incidence of tuberculosis amongst the native-born and "New Australians" arriving during the last three years, it will indicate significant past trends and provide a basis against which future trends may be gauged.

In order to determine the relative differences in tuberculosis mortality rates for native-born Australians and migrants, deaths in five-year age groups for males and females have been compared with the census population figures for 1911, 1921, 1931 and 1947. The average mortality during a three-year period around the census date was taken in order to eliminate chance variations from year to year. The rates for migrants were also examined according to their length of stay in Australia. The figures for persons of unspecified age or length of stay were averaged over the specified figures.

Total Mortality.

In both groups the mortality rate from tuberculosis was found to be declining. This decline is represented graphically in Figure I. In the period 1910 to 1912 the mortality rate for all males was nine per 10,000. By the period 1946 to 1948 this had dropped to four per 10,000. The rate for all females similarly dropped from eight per 10,000 in the period 1910 to 1912 to two per 10,000 in the period 1946 to 1948. Similar proportionate falls are exhibited if the quinquennial rates are applied to a standard population based on the 1932-1934 life table. Mortality rates for the standard population for all males fell from 10·4 per 10,000 in the period 1910 to 1912 to 4·8 per 10,000 in the period 1946 to 1948, and for all females from 7·9 per 10,000 in the period 1910 to 1912 to 2·1 per 10,000 in the period 1946 to 1948.

It is remarkable that both for males and for females, but particularly for the former, the shape of the mortality rate curve has altered and tends now to come up to a maximum during old age. It is becoming widely accepted that mortality from tuberculosis largely depends on the approximate year of birth. Thus a group of persons born in a given quinquennial period are subject to a different and higher mortality rate from a group born in a later quinquennial period. It appears that cohorts of persons born in the 1870's and 1880's are at all ages exposed to a higher mortality risk than those born in the 1910's and 1920's. The tendency for tuberculosis mortality rate curves to come to a peak in old age can be very largely explained by the higher vulnerability of the 1870-1880 cohorts, the members of which now form the old age groups (Lancaster, 1950).

If, however, the mortality experience of 1870-1880 cohorts was plotted, it would be found that there were two peaks in mortality from tuberculosis, between the ages forty to fifty years and in old age, whereas the mortality experience of previous cohorts declines after early middle age. Figure I

shows, in effect, that mortality rates for males in the old age groups in the period 1946 to 1948 were higher than those for the period 1910 to 1912, which is surprising in view of the constant overall decline in the mortality of cohorts born in succeeding periods. Similar peaks in old age for a given cohort are not yet apparent in data collected in most other countries, but have been found in Scotland. V. H. Springett (1950), who has examined the figures of various countries, attributes the phenomenon in Scotland to the effects of the war. It is difficult to see how the war could have accelerated in Australia the death of aged men from tuberculosis, and it remains to be seen from future investigations whether these high rates are of a transitory or of a lasting nature.

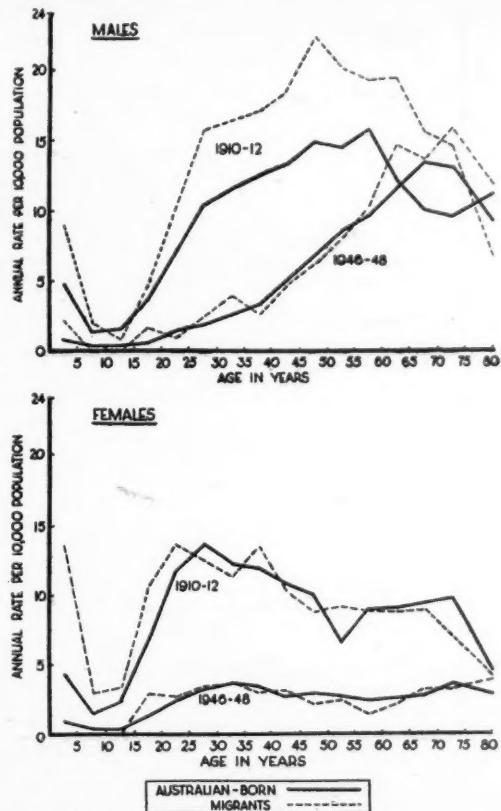


FIGURE 1.

Tuberculosis mortality rates. Australian-born persons and migrants by quinquennial age groups. Years 1910-1912 and 1946-1948.

Moreover, although there is not yet a second peak in the mortality rate of male cohorts in most other countries, there has been noted both in the United States and in England and Wales an actual increase in the rate of tuberculosis in later male age groups. The United States Public Health Service (1950) has commented on the increase in tuberculosis death rates for men aged sixty-five years and over, and has stated that the conspicuous change in trend should warrant exploration. Similar comments have been made by the Registrar-General of England and Wales (1949).

The female mortality rate for tuberculosis is highest during the child-bearing years and relatively low later in life, contrasting with high rates for middle-aged and elderly males, and so the influence of cohorts reaching old age is not so pronounced as it is with males. As a consequence female standardized mortality has declined to

26.5% of the 1910-1912 figure compared with a decline of 46% for males. In Australia there is little sign of an increase in tuberculosis mortality rates of females in the higher age groups.

Relative Mortality of Australian-born Persons and Migrants.

A higher mortality rate was noted for male migrants than for native-born Australians. In the period 1910 to 1912 the crude rates were 16.3 and 7.1 per 10,000 respectively, but by the years 1946 to 1948 the rates had declined to 7.8 and 3.5 per 10,000. On the standardized population previously described, the 1910-1912 rates were 12.8 and 9.3 per 10,000 and the 1946-1948 rates 5.1 and 4.6 per 10,000 respectively. The much greater dispersion at the earlier period is clearly shown in Figure 1. At the later date the

TABLE I.
Tuberculosis Mortality Rates: Annual Rates per 10,000 of Population.

Age Group. (Years.)	1910 to 1922.		1946 to 1948.	
	Males.	Females.	Males.	Females.
<i>Australian-born Persons.</i>				
0 to 4	4.7	4.1	0.7	0.7
5 to 9	1.3	1.3	0.2	0.2
10 to 14	1.5	2.0	0.2	0.2
15 to 19	3.6	6.5	0.5	1.1
20 to 24	7.0	11.4	1.2	2.3
25 to 29	10.3	13.4	1.7	2.1
30 to 34	11.5	12.0	2.5	2.5
35 to 39	12.5	11.7	3.2	2.2
40 to 44	13.2	10.4	4.0	2.6
45 to 49	14.8	9.7	6.7	2.7
50 to 54	14.6	6.2	8.4	2.6
55 to 59	15.6	5.6	9.6	2.2
60 to 64	12.1	5.8	11.5	2.4
65 to 69	9.9	9.1	13.5	2.0
70 to 74	9.5	9.5	13.1	2.5
75 and over	11.2	4.3	9.2	2.7
<i>Migrants.</i>				
0 to 4	8.9	13.2	2.1	—
5 to 9	2.0	2.8	—	—
10 to 14	0.7	3.1	—	—
15 to 19	4.5	10.3	1.4	0.7
20 to 24	9.7	13.3	2.9	2.4
25 to 29	15.6	12.3	2.8	2.2
30 to 34	16.4	10.9	3.8	2.4
35 to 39	17.0	13.1	2.5	2.8
40 to 44	18.2	9.9	4.6	2.8
45 to 49	22.2	8.4	6.0	1.9
50 to 54	19.8	8.9	7.9	2.3
55 to 59	19.1	8.5	10.2	1.2
60 to 64	19.3	8.5	14.6	1.9
65 to 69	15.5	8.7	13.6	3.0
70 to 74	14.5	6.8	15.8	3.2
75 and over	6.6	4.0	11.7	3.8

rate for migrants was in fact significantly greater than that for Australian-born persons only for the groups aged fifty-five years and upwards. The higher rate for migrants at the later date may have been a residual effect of the possession by cohorts of migrants of greater vulnerability to death from tuberculosis than native-born Australians, and it therefore appeared that the relatively excessive tuberculosis death rate for male migrants was being eliminated. Such a conclusion would, however, have to be reviewed at a later date when the mortality of post-war migrants could be examined. In this connexion reference may be made to the report of a Mantoux survey of "displaced person" migrants' children by J. P. Van Leent and P. F. Hopkins (1951). This report noted the much higher percentage of positive reactors among these children than among white children born in Australia, and expressed the opinion that the numerous positive reactors constituted a group of potential "breakdown" cases. Displaced persons under the International Relief Organization scheme arrived in Australia from the end of 1947, but the bulk reached our shores in 1949 and 1950.

Up to the age of twenty-five years, female migrants in the period 1910 to 1912 showed a consistently higher death

rate than did native-born Australians; but above that age there was a close correspondence between the rates. By the years 1932 to 1934 there was little difference between the rates for young migrants and Australian-born persons. Figure I reveals an excess rate of migrant deaths in the fifteen to nineteen years age group during the years 1946 to 1948, but no migrant deaths at all under the age of fifteen years, and there is clearly no significant difference between standardized death rates of female migrants and Australian-born persons in these years.

The mortality rates of migrants were also computed for three or four groups whose length of stay was less than twenty years and for those who had been in Australia

Summary and Conclusions.

Standardized tuberculosis mortality rates have declined steadily from 1910-1912 to 1946-1948, the decline being more pronounced for females than for males. The male rate is influenced by mortality in the advanced age groups, which, after having decreased, has started to increase. This mortality for aged males is higher than would be expected as a residual of high vulnerability in the cohorts reaching these ages in the period 1946 to 1948.

In the years 1910 to 1912 tuberculosis mortality rates of male migrants were significantly greater than those for native-born male persons. In the case of females the migrant rate up to the age of twenty-five years was con-

Age Group. (Years.)	Tuberculosis Mortality Rate Indices. (1910-1912 and 1920-1922 Rates Combined = 100.)			
	1932 to 1934.		1946 to 1948.	
	Males.	Females.	Males.	Females.
<i>Australian-born Persons.</i>				
0 to 9	41	61	19	30
10 to 19	38	42	14	19
20 to 29	48	62	17	25
30 to 39	57	61	26	33
40 to 49	87	47	42	30
50 to 59	88	54	65	38
60 to 69	80	63	96	41
70 and over	92	74	143	60
<i>Migrants.</i>				
0 to 19	61	63	35	32
20 to 29	42	52	15	28
30 to 39	51	62	20	31
40 to 49	54	65	29	31
50 to 59	77	47	50	24
60 to 69	70	58	84	34
70 and over	92	74	145	84

twenty years or more. As a general rule there were no significant differences in mortality rates of recently arrived migrants and those whose stay had been of longer duration. Owing to the small populations in the groups the sampling errors were large. However, in the period 1946 to 1948 it was possible to state that the male groups aged twenty-five to thirty-nine years had a higher mortality rate among recent arrivals than among those persons who had arrived in Australia when infants.

Figure II shows a comparison between mortality rates of the periods 1932 to 1934 and 1946 to 1948, and the combined rate of the earlier periods 1910 to 1912 and 1920 to 1922. Owing to the small populations in the migrant groups aged 0 to nine years and ten to nineteen years, the figures for these groups were combined. In both of the periods charted the indices were generally low in the early age groups and increased with age. Male indices started to increase steeply at earlier ages than female indices, and by the years 1946 to 1948 the curve for males was hyperbolic in shape and reached an index of 143 for the highest age group of persons aged over seventy years. In this connexion it is noteworthy that the rate for the higher male age groups had declined in the period 1920-1922 from its 1910-1912 level; by the period 1932-1934 it had risen again somewhat but was still below the 1910-1912 level. In the years 1946 to 1948 it exceeded the 1910-1912 level.

For males aged twenty to seventy years the index for migrants ran at a lower level than that for other persons, indicating that the death rate for male migrants in this important age group had decreased more than that for native-born persons, and so the difference between the two rates had narrowed.

The rates for native-born Australians used in this paper exclude the aboriginal population. It is of interest to note that the percentage of positive reactors to Mantoux tests among aboriginal children in Queensland has recently been found to be comparable to that amongst "displaced person" migrant children (State of Queensland, 1951).

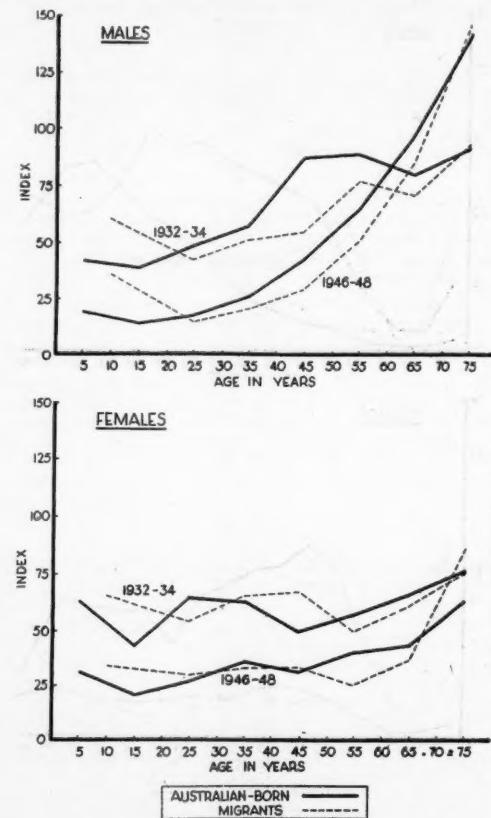


FIGURE II.
Tuberculosis mortality rates. Australian-born persons and migrants by decennial age-groups; 1910-1912 and 1920-1922 rates combined = 100.

sistently higher than that for Australian-born persons. By the years 1946 to 1948 the rate for male migrants was significantly higher than that for native-born Australians only in persons aged fifty-five years and upwards, and there was no significant difference between the rates for migrants and for native-born females. Rates for native-born persons exclude aborigines.

In the period 1946 to 1948 male migrants, aged twenty-five to thirty-nine years, had a significantly lower rate if they had been in Australia twenty years or over than if they had not; but otherwise length of stay could not be shown to be relevant to tuberculosis mortality rates.

Indices for 1932-1934 and 1946-1948 with 1910-1912 and 1920-1922 rates as a base revealed that for males rates for the earlier age groups had decreased more than those for later age groups. By the period 1946 to 1948 rates for older males had, in fact, increased over those for the base

period. Rates for migrants aged twenty to seventy years had decreased more than those for Australian-born persons. For females indices increased slightly with age, but very much less so than for males, and in all cases they remained substantially below those for the base period. Indices for migrants were in general not significantly different from those for native-born persons; but the figures examined do not include the bulk of migrants brought out since the war.

Acknowledgements.

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Reports of Cases.

OSTEITIS DEFORMANS INVOLVING THE JAW.

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OSTEITIS DEFORMANS was first described by Paget in 1877, and is often referred to as Paget's disease of bone. According to Price (1938), "the disease may affect the head, the clavicles, the bones of the thorax, the spine and the long bones; the bones affected in order of frequency being skull, tibia, femora, pelvis, spine, clavicles, ribs and radii".

Most text-books of pathology, medicine and surgery describe the advanced stages of the disease. Boyd's (1934) description is as follows: "The patient has short squat figure, with bent shoulders, curved back, sunken chest, long arms, and a great head hanging forward: he waddles along with bowed legs, out-turned toes, and with the aid of a stick."

Bailey and Love (1938) give the following clinical features:

1. Pain is the most constant symptom, and is usually complained of for years before the cause is realized. The tibia is one of the first bones to be affected, and the disease may remain localized in a single bone for years.
2. Diminution of stature, even up to thirteen inches, due to kyphosis and bending of the long bones of the legs.
3. Increased diameter of the head, an early indication of which may be the necessity for larger hats.
4. Spontaneous fracture is not uncommon.

In recent years, however, there has developed an awareness that the disease may exist in a much milder and sometimes subclinical form, and may in some cases affect chiefly or only the bones of the head. Schmorl (quoted by Bailey and Love) stated that 3% of persons aged over forty years are affected with the disease, although obvious signs are often not noticeable for many years. Thoma (1944) states that the jaw often shows changes before symptoms appear in the rest of the skeleton. He has reported four cases of typical Paget's disease involving the maxilla. In a review of the literature he quotes other writers who have described the disease as it affects the jaws and teeth:

The teeth are very frequently affected by the involved surrounding bone. Hypercementosis has been reported by Fox (1933), Seldin (1933), Cahn (1937) and Stafne and Austin (1938) who all found a slight to excessive amount of cementum on one or several teeth in 18 out of 23 patients whose jaws were involved.

Stafne and Austin (1938) report the findings of 138 cases of Paget's disease at the Mayo Clinic. There was radiographic evidence of the disease in the jaws in 23 (or 16.6%) of these cases, mostly the maxilla, the mandible being involved in only three. These writers state that "Paget's disease has been considered relatively rare, but this is probably attributable to the fact that only the more advanced forms of the disease have been recognized".

In two cases recently described by Rushton (1948), the disease involved the maxilla and the skull; in one case in addition osteoporosis of the mandible, spine, pelvis and long bones was present. In the other case the bony swelling in the maxilla was on one side only; diffuse sclerosis was found in both molar regions of the mandible, typical changes were found in the calvarium, and some early changes were present in the left ischium.

Acharya (1950) has recently reported a case in which there was gross enlargement of the maxilla. In the skull the typical "cotton-wool" appearance was present, and in both femora and in the pelvis radiographic changes were found.

Pathology.

Although the term "osteitis" is applied to this disease, no evidence has yet been found to indicate an infective inflammatory condition. The bones undergo partial resorption and replacement with bone of a different type in excessive amount. The resultant bone is lighter in weight and softer than normal, though greatly increased in thickness. These changes are often pronounced in skull bones, great thickening taking place with obliteration of the diploe, and as was mentioned earlier, a characteristic complaint of the patient is that he has to keep buying larger sizes in hats.

Other clinical signs such as bowing of the legs, kyphosis *et cetera*, are the direct result of the bony changes typical of the disease.

Histologically there is an increase of finely trabeculated cancellous bone alternating with patches of normal bone and areas of fibrous tissue.

Somewhat parallel changes—that is, resorption and replacement—occur in the teeth when the jaw bones are affected.

Rushton (1938) made a study of teeth from an elderly patient suffering from this disease. These were affected by excessive hypercementosis, and there was evidence of considerable and repeated previous resorption of portions of the tooth roots.

Clinical Record.

The case here described is that of a female patient, aged sixty-two years. She consulted her dentist complaining of some vague discomfort, hardly amounting to true pain, in the upper jaw. He took radiographs of the maxillary teeth in the areas complained of. These revealed the following abnormalities: (i) irregular resorption of the roots of the two central incisors, with the production of areas having a radiographic appearance of caries; (ii) hypercementosis of the roots of the following teeth: the canine and the first and second premolars on the right side and the first premolar on the left side; (iii) irregular calcification of the jaw, some areas showing increased deposition of calcium, other parts showing resorption; (iv) abnormally small marrow-spaces which are separated by fine trabeculae. Films of the mandible revealed no abnormality.

The patient was referred to the writer on April 30, 1948. The whole of the maxilla appeared enlarged, the maxillary teeth were prominent, and the lips could be closed only with effort. Her dentist and her relatives had been aware for some years of the prominence of the upper jaw.

A provisional diagnosis of *osteitis deformans* was made. However, further physical examination revealed no other

signs or symptoms of the disease. The patient was emphatic that she suffered from no pains in any part of the body other than the vague discomfort in the jaw referred to above. She denied that her head was increasing in size, and physical examination revealed no changes characteristic of *osteitis deformans* in the limbs or spine. For several years she had suffered from thyrotoxicosis, but for some time she has been receiving treatment which quite controls the condition. There were no other relevant factors in her medical history.

The following further radiographs were taken: (i) intra-oral films to show as much of the maxilla as possible; (ii) films of the cranium and the long bones.

The films of the maxilla confirmed the opinion that the bony changes extended far into the substance of the maxilla, with obvious diminution in the size of the antra. The films of the skull showed the typical appearance of Paget's disease, with increased thickening of the cortex and numerous dense areas producing the so-called "cotton-wool" appearance.

Unfortunately the patient refused to have radiographs taken of the long bones. As has previously been mentioned, however, she had submitted to physical examination, which disclosed no abnormality in the extremities or spine.

No treatment was advised, as no cure for the disease is yet known. The patient was warned that if complete extraction of the maxillary teeth became necessary, an extensive alveolectomy would have to be performed before she could be fitted with a denture.

Summary.

A case is described of *osteitis deformans* (Paget's disease), evidently of long standing, in which clinical signs of the disease are conspicuous only in the maxilla, and which is not evident in any parts of the body other than the maxilla and cranium. It is recognized, of course, that some degree of pathological change might have been detected radiographically in other bones had the patient consented to have additional radiographs taken.

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Reviews.

A TEXT-BOOK OF MEDICAL OPHTHALMOLOGY.

"SYSTEMIC OPHTHALMOLOGY" is a collective work of British and American ophthalmologists and physicians offering interpretations of ophthalmic changes in systemic disease. Arranged by Arnold Sorsby, it resembles the volumes of "Modern Trends in Ophthalmology" previously presented by the same editor and publishers. It should obtain an equally appreciative reception.

Thirty-eight contributions are arranged in six sections devoted to the following subjects: prenatal pathogenic influences; inflammation, allergic reactions and infections;

¹ "Systemic Ophthalmology", edited by Arnold Sorsby; 1951. London: Butterworth and Company (Publishers), Limited. 10" x 7", pp. 748, with 38 plates in colour and 309 illustrations. Price: £5 5s.

nutritional, metabolic and endocrine disturbances; central nervous system; cardio-vascular and haematopoietic systems; general disturbances. The papers have been written by specially selected authorities recognized by their own contributions in the particular subjects. Each chapter has a selected bibliography facilitating reference to the important original papers.

This should be a very useful text-book for senior ophthalmology students and it contains many helpful references for consulting physicians, but much of the subject matter would probably be very difficult for an ophthalmologist during his early studies. Practising ophthalmologists will find of immediate practical value the chapters on allergy, chronic bacterial infections and dermatoses with ocular manifestations. A description of the pathogenic fungi and fungous diseases considerably enlightens an extremely difficult subject. Ophthalmic features of tropical diseases receive due emphasis. Unfortunately, no text-book can be presented describing the latest therapeutic procedures, and this book contains only an occasional reference to cortisone, ACTH and the newer antibiotics.

The 300 half-tone illustrations contain many very clear and instructive clinical photographs, but several of the X-ray film reproductions and a fundus photograph of angioid streaks show insufficient detail. Thirty-eight coloured plates (mainly from fundus paintings but including some clinical photographs in colour) are of particular merit. Printer's errors were difficult to find, but a few were noticed in the chapter on acquired syphilis and on page 525 "arteriolar sclerosis" appears twice as "arteriolar necrosis".

"Systemic Ophthalmology" should gain recognition as one of the important current text-books of ophthalmology.

MASSEAGE AND MEDICAL GYMNASTICS.

THE fourth edition of "Massage and Medical Gymnastics" has been revised by Miss E. M. Tod since the death of the original author, Miss Mary V. Lace.¹ The standard set in the previous editions has been well maintained. Part I opens with many useful tips to the physiotherapist on the approach to and management of patients. This is followed by a detailed account of the indications, contraindications and methods of applying various forms of massage. Part II deals with medical gymnastics. The modern tendency is to use more active and less passive movements in treatment. This has been stressed by Miss Tod, and many of the passive exercises appearing in the previous editions have been deleted. The object of all movements and exercises is restoration of function, and full details of the methods to be used in obtaining this restoration in the various body structures are clearly set out and are well illustrated by diagrams. A sound understanding of anatomy and physiology is essential for a proper understanding of the methods advised.

A YEAR BOOK OF OBSTETRICS AND GYNAECOLOGY.

THE editorial comments of J. P. Greenhill are a valuable feature of "The 1951 Year Book of Obstetrics and Gynaecology".² He avoids trite and routine remarks and presents many abstracts without comment; but when he offers commendation or condemnation, adds a summary of a large or widely discussed subject or recounts some relevant personal experience, his wide knowledge is apparent. The section on obstetrics covers pregnancy, labour, the puerperium and the newborn. Pregnancy is dealt with under the headings of physiology, abortion, ectopic pregnancy, complications and toxæmia. The term "physiology" is interpreted broadly in the material included; the heading might well have been "physiology and pathology" or just "miscellaneous". The abstracts collected on the subject of toxæmia show the extensive effort being made to determine the underlying bodily changes and aetiology and to find a rational mode of therapy. The subsection on labour is

¹ "Massage and Medical Gymnastics (Mary V. Lace)", revised by E. M. Tod, M.C.S.P., T.M.M.G., with a foreword by James Mennell, M.A., M.D., B.Ch.; Fourth Edition; 1951. London: J. and A. Churchill, Limited. 8½" x 5½", pp. 234, with 103 illustrations. Price: 18s.

² "The 1951 Year Book of Obstetrics and Gynaecology (August, 1950-June, 1951)", edited by J. P. Greenhill, B.S., M.D., F.R.C.S.: 1951. Chicago: The Year Book Publishers, Incorporated. 8" x 5½", pp. 568, with 134 illustrations. Price: \$5.00.

divided into general material, analgesia and anaesthesia, complications, operative obstetrics and uterine haemorrhage. Relief of pain is prominent. Caesarean section continues to be a topic of interest. Uterine haemorrhage provides the occasion for some thoughtful practical comments by the editor. The intense interest and the progress made in improving the lot of the newborn is well brought out.

The section on gynaecology has subsections on general principles, diagnosis, infertility, operative technique, infections, benign tumours and endometriosis, special ovarian tumours, malignant tumours, menstrual disorders and endocrinology. Operative technique receives particularly generous treatment (to the extent of 70 pages) with good illustrations and annotations. Careful attention is paid to the problems of early diagnosis of cancer and its treatment.

In both sections a wide range of literature is covered. The editor's selection has been careful, though not just to support his own views; in places he expresses strong and even scathing disagreement with views or work reported. The volume, which is as well produced as ever, should have a wide appeal and usefulness.

ENDOCRINOLOGY.

THE second (revised) edition of "The Practice of Endocrinology" achieves Dr. Raymond Greene's object of providing a book of value to the general practitioner. The approach is essentially practical and reflects the wide clinical experience of the contributors. The index comprises 10% of the book; this, with the detailed table of contents, aids quick reference. The large print, short paragraphs, frequent sub-headings and lucid style make reading easy. Errors are negligible. The bibliography has been curtailed, but it could be reduced further and be confined to texts accessible to the general practitioner.

RELIEF OF PAIN IN CHILDBIRTH.

SAFE and satisfactory analgesia and anaesthesia in obstetrics is the theme of a little book entitled "Relief of Pain in Childbirth" by Nixon and Ransom.¹ After stressing the all-important psychological preparation for labour during the antenatal period, the authors discuss and assess the various methods applied today to mitigate the sufferings of women in labour. The administration, dosage and effects of common drugs are described in sufficient detail, while the frequently forgotten distinction between analgesics and hypnotics is emphasized. One chapter is devoted to a discussion on sedation in normal labour, another to suggestions for the appropriate drugs to be given in various types of abnormal labour. The book ends with the authors' well-considered opinion on resuscitation of the newborn. This little work should be extremely useful to practitioners and teachers alike.

A YEAR BOOK OF PEDIATRICS.

MORE purely editorial material is included in "The 1951 Year Book of Pediatrics" than is in some other members of the Year Book series.² It includes a brief but thoughtful and informative introductory article entitled "The Year in Pediatrics" and introductions to the main chapters summarizing progress in the subject concerned, as well as the customary comments and criticisms accompanying many of the individual abstracts. The result with the comprehensive material abstracted is particularly satisfactory. Chapters are devoted to the premature and the newborn, nutrition

¹ "The Practice of Endocrinology", edited by Raymond Greene, M.A., D.M., M.R.C.P.; Second Edition; 1951. London: Eyre and Spottiswoode. 10" x 6½", pp. 412, with 56 plates and 25 text figures. Price: 65s.

² "Relief of Pain in Childbirth: A Handbook for the General Practitioner", by W. C. W. Nixon, M.D., F.R.C.O.G., and Shila G. Ransom, M.R.C.S., L.R.C.P., D.A.; 1951. London: Cassell and Company, Limited. 7½" x 5", pp. 116, with 13 illustrations. Price: 7s. 6d.

³ "The 1951 Year Book of Pediatrics (July, 1950-June, 1951)", edited by Henry G. Poncher, M.D., with the collaboration of Julius B. Richmond, M.D., and Isaac A. Abt, M.D.; 1951. Chicago: The Year Book Publishers, Incorporated. 8" x 5½", pp. 442, with 89 illustrations. Price: \$5.00.

and metabolism, the gastro-intestinal, genito-urinary and respiratory tracts, infectious diseases and immunity, allergy, poliomyelitis, tuberculosis, the heart and blood vessels, blood, endocrinology, orthopaedics, dermatology, oto-laryngology, ophthalmology, neurology and psychiatry, therapeutics and toxicology, and miscellaneous subjects. A notable feature is the number of tables which summarize and present in readily accessible form important data and essential points from papers abstracted. It is not always clear whether these tables are taken from the original papers or have been compiled by the editor, but they certainly add to the practical usefulness of the volume. It deserves the attention of all practitioners who have to do with the health of children.

PORCINE DEVELOPMENT.

SOME 900 years ago students at the Salerno Medical School dissected the pig as a reasonable substitute for man. However, Professor Patten's book, "Embryology of the Pig", is not intended as a substitute for human embryology. Indeed, there are now plenty of excellent books on that subject, including one by Patten himself. The "Embryology of the Pig" is designed to provide a good grounding in mammalian embryology such as a student of general zoology would desire. The book certainly fulfils such a purpose, for it has become widely known and appreciated, and is now in its third edition. In these intense times, unfortunately, it is unlikely that a work which is not directly applicable to the study of medicine will enjoy the popularity it deserves. That is a pity, because works of the type under review are virtually monographs in their own right: they have a high scientific value and are all too few. As might be expected from Professor Patten's wide experience and high reputation, this work is authoritative and based upon ample material. At the same time it is clearly written and lavishly illustrated with excellent figures that supplement the text admirably. The bibliography is well selected, the index is good and typographical errors are few. The binding and general appearance are attractive and, taking all things into account, the price is not unreasonable for these times. The work can be strongly recommended to every student of zoology, and certainly it should find a place in every zoological, medical and veterinary library.

FRACTURES, DISLOCATIONS AND SPRAINS.

THE special feature of Key and Conwell's book, "The Management of Fractures, Dislocations and Sprains",³ is that the authors describe several methods of treating the same fracture, and doubtless this is one of the reasons for the popularity that it has earned; but this wide choice that is left to the reader appears, in some instances, to have disadvantages. For example, for fractures of the fingers (phalanges) the splints that are recommended include a wooden tongue depressor, metal finger splints, large roller bandage and a wooden ball; unfortunately none of these is satisfactory. If traction is necessary the reader may select from four procedures. For skeletal traction there are three courses, and one of these is by means of a towel clip; but skeletal traction should not be used unless the fracture is compound. The three principles of splinting fractures of the phalanges (except a crushed tip of the terminal phalanx) are that the wrist and metacarpo-phalangeal joint should be immobilized, in order to prevent the long flexors and extensors and the lumbricals and interosseous muscles from causing displacements; the affected finger should be semiflexed; and the good fingers and thumb should not be immobilized but fully used. The use of a straight tongue spatula does not permit semiflexion, and the wrist is not immobilized; balls or bandage rolls used as splints immobilize the good fingers as well as the affected one and may cause stiffness in all the fingers, and late permanent disabilities from adhesion have resulted from this method.

¹ "Embryology of the Pig", by Bradley M. Patten; Third Edition; 1948. Philadelphia: The Blakiston Company. London: George Allen and Unwin, Limited. 9½" x 6½", pp. 366, with 187 illustrations, six in colour. Price: 35s.

² "The Management of Fractures, Dislocations and Sprains", by John Albert Key, B.S., M.D., and H. Earle Conwell, M.D., F.A.C.S.; Fifth Edition; 1951. St Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 10½" x 7½", pp. 1232, with 1195 illustrations. Price: £8 8s.

which is to be condemned. On the other hand it is an advantage to have described the various methods of treating fractures of the femur, tibia and fibula *et cetera*, and this has been done at length.

This is the fifth edition since the book with its 1200 odd pages and the same number of illustrations was published in 1934 (the fourth edition was reprinted in 1947), having been written for the student, the general practitioner and the surgeon. The purpose is to provide a working guide with practical details of technique, and these are adequately provided in the pictures and text. For example, the authors wisely do not advise skin-tight plasters for fresh fractures which may be followed by swelling (and that applies to all), they point out the danger of the improper use of crutches that cause radial nerve paralysis, and the treatment of compound and infected fractures is dealt with at length. Internal fixation with plates *et cetera* is advised under certain conditions for compound fractures, but this may advisedly be left to experts. The ordinary surgeon would be safer using orthodox external splints, but the authors are not inclined to express forcible opinions anywhere on this or other disputed subjects.

In the chapter on complications, so-called Sudeck's disease is described as a curious complaint that has never been produced experimentally; but the common view now is that it is more likely to be a grand example of successful malingering, or the effects of disuse atrophy in an honest but timid and elderly patient. The late result of prolonged immobilization of the hand or foot, whether assumed with the dishonest purpose of making a claim for permanent disability or from any other cause, is the same—namely, stiffness of the fingers and adhesions in the tendon sheaths. These changes may be permanent if the pretence has been kept up too long; but they often clear up reasonably soon after a lump sum settlement.

There are long chapters on skull and jaw injuries. The special method of radiography of the zygoma is new and appears to have merit. Gillies' method of elevation of a depressed malar bone through the temporal incision is described, but this method is liable to cause bleeding from the temporal vessels or even facial paresis. However, insertion of a long-handled sharp hook under the lower margin of the depressed malar is a neat, quick, simple and safer method, and the puncture mark soon disappears.

The chapter on the spine is very comprehensive and helpful. A discussion of pain in the back is included, and the results of 310 disk operations are given: 41% of patients operated on had no pain or disability, and 48.4% had intermittent pain which would not be considered satisfactory in a workers' compensation court. However, these results appear to represent a true picture of the outcome of the operation, and not the 90% of good results that some surgeons claim. In these circumstances it would be advisable for those surgeons who favour early and frequent operations in these cases to examine their consciences.

The important and difficult Monteggia fracture-dislocation of the elbow is not dealt with at much length, but fractures of both forearm bones are dealt with in a complete manner.

The Whitman method of treatment for intracapsular fractures has been outmoded and is as dead as the dodo; nevertheless, a long description of it is given in eight pages. The authors state that "if a surgeon who is familiar with the operative method is not available, the abduction method of Whitman is the method of choice". But it would be a piece of bad luck for a patient to be placed in that position; he would be as unfortunate as the individual who develops acute appendicitis in the Antarctic or on a cargo ship not carrying a ship's surgeon.

Some of the illustrations are not so good as others, although they are effective. On the whole this book should provide a guide for those for whom it has been written.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Wounds of the Extremities in Military Surgery", by Oscar P. Hampton, Jr., M.D., F.A.C.S.; 1951. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 10" x 7", pp. 484, with 181 illustrations. Price: £5 5s.

Basic principles of military surgery by an orthopaedic surgeon with extensive military experience.

"New Outlook on Mental Diseases", by F. A. Pickworth, M.B., B.S., B.Sc.; 1952. Bristol: John Wright and Sons, Limited. 11" x 7½", pp. 304, with 41 illustrations, some in colour. Price: 60s.

The author is a pathologist. His ideas, which are original, are aimed at defining "the medical aspects of the mind and its disorders".

"Essentials of Neurosurgery", by Leslie C. Oliver, F.R.C.S. (England); 1952. London: H. K. Lewis and Company, Limited. 9" x 6", pp. 206, with 50 illustrations. Price: 25s.

Intended as a guide to neurosurgeons in training and as an aid to candidates reading for higher surgical examinations.

"The Organization of the Sixth International Congress of Radiology: London, 1950", published under the authority of the British Executive Committee; 1951. London: H. K. Lewis and Company, Limited. 9" x 6", pp. 44. Price: 3s. 6d.

Compiled as a permanent record of the proceedings and to provide information which may be of value to organizers of similar meetings.

"A Practical Handbook of Midwifery and Gynaecology for Students and Practitioners", by W. F. T. Hautain, O.B.E., M.C., B.A., M.B., B.Ch., F.R.C.P.Ed., F.R.C.S.Ed., F.R.C.O.G., and Clifford Kennedy, M.B., Ch.B., F.R.C.S.Ed., F.R.C.O.G.; Including a Section on the Management of the Infant and Neo-Natal Conditions by J. L. Henderson, M.D., F.R.C.P.Ed.; Fourth Edition; 1952. Edinburgh: E. and S. Livingstone, Limited. 8½" x 6", pp. 422, with 47 illustrations. Price: 24s.

Extensively revised since the issue of the previous edition four years ago.

"Fractures and Joint Injuries", by Reginald Watson-Jones, B.Sc., M.Ch.Orth., F.R.C.S., F.R.A.C.S. (Hon.), F.A.C.S. (Hon.); Fourth Edition; Volume I; 1952. Edinburgh: E. and S. Livingstone, Limited. 10" x 7", pp. 368, with 709 illustrations, many in colour. Price: £6 per set of two volumes.

Completely revised and largely rewritten with much new material added.

"The Specialties in General Practice", edited by Russell L. Cecil, M.D.; 1951. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 10½" x 7½", pp. 834, with 470 illustrations. Price: £6 17s. 9d.

Contains 14 chapters, each on a special subject, written by a distinguished authority especially for the general practitioner.

"Blood Clotting and Allied Problems: Transactions of the Fourth Conference, January 22-23, 1951, New York", edited by Joseph E. Flynn; 1951. New York: Josiah Macy Junior Foundation. 9½" x 6½", pp. 272, with 81 illustrations. Price: \$4.00.

Contains papers with discussions on the direct investigation of factors leading to thrombosis, canine haemophilia, characteristics of blood platelets and their significance in thrombus formation, morphological and physiological studies of platelets and haemostasis, antithrombin and α -tocopherol, the transition of fibrinogen to fibrin and polarographic studies of the fibrinogen-fibrin reaction.

"Biological Antioxidants: Transactions of the Fifth Conference, November 30-December 1, 1950, New York", edited by Cosmo G. Mackenzie; 1951. New York: Josiah Macy Junior Foundation. 9½" x 6½", pp. 280, with six illustrations and about 25 text figures. Price: \$3.75.

Contains papers with accompanying discussions on chemical changes produced by radiations, radiation effects on higher animals, the effect of ionizing radiations on sulphhydryl systems, genetic effects of irradiation and irradiated broths, peroxides and mutations, and free radicals, peroxides and antioxidants in some biological processes.

"The American Illustrated Medical Dictionary: A Complete Dictionary of the Terms Used in Medicine, Surgery, Dentistry, Pharmacy, Chemistry, Nursing, Veterinary Science, Biology and Medical Biography with their Pronunciation, Derivation and Definition", by W. A. Newman Dorland, A.M., M.D., F.A.C.S.; Twenty-Second Edition; 1951. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 10" x 7", pp. 1762, with 720 illustrations. Price: £5 9s. 8d.

The previous edition was published in 1947.

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The Medical Journal of Australia

SATURDAY, APRIL 5, 1952.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

A LITERARY JUBILEE.

If the author of Ecclesiastes had lived today, he would probably have added to his statement that of making many books there was no end something about the colossal task of reviewing them. We all know that in the days of The Preacher the making of books was indeed a laborious business; even today, with our modern type-setting machines, our splendid process engraving, and our rapid printing presses, it is still a laborious business to make a book. Men and women write books for all kinds of reasons, and the best of all reasons is probably that they have no reason at all. People who buy books, or shall we say, who acquire them, generally have a reason for their choice, and this is why the reviewing of books has become such an enormous business. One of the most important publications in the English-speaking world that deal with books is *The Times Literary Supplement*. On January 18, 1952, the fiftieth anniversary number was published. The subtitle of this number describes it as an "historical survey and selection from the criticisms of fifty years". All lovers of books—and the medical profession has in its ranks many who may be so described—will be interested in this publication.

The story of the early days of *The Times Literary Supplement* begins with the statement that "like some other English things, it was started as a makeshift and continued through an oversight". We read that in 1901, *The Times* was printing every year about 262 columns of reviews, of which 55 columns were given up to novels. In 1897, the magazine *Literature* was founded; but though it was published from *The Times* office, it was an entirely separate journal and gave no relief to the pressure on the space of the paper. The publication of reviews in the columns of *The Times* was "interesting and profitable",

but it was found that while Parliament was sitting, reviews of books were crowded out. It was therefore resolved to publish these reviews in an occasional supplement. On Friday, January 17, 1902, there appeared the first issue of the *Literary Supplement of The Times*. An official announcement was made that during the parliamentary session, literary supplements to *The Times* would appear as often as might be necessary in order to keep abreast of the more important publications of the day. Parliament adjourned for Easter on March 27. *The Literary Supplement* was published as usual on Friday, March 28, and on Friday, April 4—there had been no preparation to take back into the paper the matter of which the supplement had been relieving it. The management had forgotten about it and the member of the editorial staff in charge of the supplement was in no hurry to remind them. Thus both the makeshift and the oversight were perpetrated. Before long *The Literary Supplement* had a larger circulation by several thousands than the daily issue of *The Times*. A mild war took place between *The Times* and certain book publishers. In October, 1906, the following notice was published: "In consequence of our insistence upon our rights to offer to our subscribers, at a reduced price, secondhand copies of books when available, some publishers have refused to supply copies of certain books to 'The Times Book Club' on the regular trade terms. At the head of each review of such books we draw attention to this notice . . ." A month or two later the announcement was replaced by a note attached to the review of any book to which it was applicable, stating that the publishers of the book declined to supply "The Times Book Club" with copies on ordinary trade terms and asking subscribers to abstain from ordering it "so far as possible". The end of the war took place in October, 1908, but all through it the publishers had steadily continued to send their books for impartial review to *The Literary Supplement*. During its twenty-first year, *The Literary Supplement* narrowly escaped extinction. *The Times* had been bought by Lord Northcliffe, and *The Literary Supplement* of March 30 was almost ready for press, when the Noble Lord issued a sudden order to the effect that the next number but two was to be the last. This death sentence was to be published immediately. It appears that an earlier threat of the same kind had been stayed by the skilful opposition of Reginald Nicholson, who was then manager. This time there appeared to be no hope. What is known as a "box" was prepared and inserted into the leading article on the front page, announcing in italic type that the issue of April 13 would be the last number of *The Literary Supplement* to appear. The author of the article who tells this story appears not without humour, for he points out that the leading article dealt with "Condorcet and Human Progress" and that the writer, Sir J. G. Frazer, linked Condorcet's book with Raleigh's "History of the World" and some other writings as "compositions born under sorrowful circumstances". But once again the journal was to owe its continued existence to something like an oversight. The order of annihilation had not penetrated into every department concerned. In one quarter there was doubt about its validity, and only twenty minutes before the number went to press the "box" was removed from the front page. The issue of April 13, which was to have been the last, duly appeared, and the leading

article on the front page was entitled "The Dying Life of a Poet". The number showed no sign of its narrow escape. The next summer, we are told, Lord Northcliffe became too ill to take an active part in his business and in August of that year he died. On August 31 *The Literary Supplement* published a long letter from Charles Whibley on Lord Northcliffe as "at all ages an eager and assiduous reader". This interesting story is now only an incident in the history of the paper, but apparently no one knows why Lord Northcliffe wished to kill *The Literary Supplement*. One incident which should be recorded is the fact that in October, 1922, the honorary degree of Doctor of Letters was conferred by the University of Leeds upon Bruce Richmond, editor of *The Times Literary Supplement*. Professor G. S. Gordon, who presented Richmond to the Chancellor, remarked that it had been the practice of the best literary editors in the country to conceal themselves behind their journals. But he held that a point might be reached when the most unselfish of editors should be invited to emerge and endure the publicity of recognition.

As most readers know, the reviews in *The Times Literary Supplement* are anonymous. In this special number anonymity is lifted in regard to the earlier years of the publication. Many books and their reviewers are named, and some of the reviews of books which appeared in the early years of the century are reproduced. Lovers of English literature will find these of absorbing interest. Argument has always taken place on the merits of signed and unsigned reviews. These arguments need not be reproduced in this place. We ourselves, in THE MEDICAL JOURNAL OF AUSTRALIA, have always been content to follow the lead of *The Times Literary Supplement* and other responsible journals. *The Times Literary Supplement* attempts "to set the limits of a permissible tone of voice, and within those limits to allow the maximum variation in order to give as much freedom as possible to the writers . . . who consent to give their anonymous services". The onus is, of course, on those who set the limits of the permissible tone of voice, in other words, the editor. We read with interest that the art of criticism, like prophecy, is inseparable from howlers, and again that the art of urbane criticism is in constant risk of tepidity. It is pointed out, however, that the real risk to a periodical critical journal today does not lie in its errors of opinion. It lies in the economic threat which hangs over the heads of its contributors. Forty or fifty years ago reviewers were able to maintain their standards of perception and detachment on a modest income "eked out by turning in articles written with affection". No one who cares for the future of literature can envisage the next fifty years "without hearing the voice of the calendar admonishing John Gilpin to

... stop and eat, for well you may
Be in a hungry case."

This applies in some measure to the reviewing of medical books, but need not be pursued further. The present object is to draw attention to the jubilee of a paper which publishes nothing but reviews and general literary criticism. All lovers of English literature will wish the paper well for the future, and we have no doubt that they will continue to derive both pleasure and profit from it.

Current Comment.

NEUROCIRCULATORY SYNDROME.

THE attitude of the medical profession to the problem now usually called "effort syndrome" or, more imposingly, "neurocirculatory asthenia", has undergone striking changes during the last generation. It has always been recognized that the syndrome, if it may truly be called one, comprises both circulatory and nervous symptoms: formerly, undue and indeed harmful emphasis was laid on the somatic symptoms; latterly the tendency has been to regard the condition as a type of circulatory neurosis. Where once oversimplification of a diagnostic label caused error which has been exposed by modern cardiology, there seems now a certain danger that we may be again oversimplifying our concepts in making no distinction between the anxiety and circulatory types of psychoneuroses. This idea is pursued by Henry H. W. Miles and Stanley Cobb in an article in which they show how overlapping of these types may occur, and how the problems of diagnosis and treatment are not solved by thinking of neurocirculatory asthenia as just one variety of neurosis.¹ Miles and Cobb refer to the recent work of Wheeler and his colleagues, who regard effort syndrome and anxiety neurosis as synonymous, and group their cases simply on a basis of common symptoms. The last-mentioned writers define their syndrome by a constellation of familiar symptoms, of which the most significant form a diagnostic triad. These are palpitation and pain in the chest; nervousness, dizziness, faintness and other similar attacks; and fatigue, with limitation of activity. Miles and Cobb make it clear that they do not object to the label thus placed on the condition, but to the concept upon which this depends. They point out that if neurocirculatory asthenia is defined solely by a list of symptoms it constitutes no nosologic entity, and they doubt if it is just to assume that all the included disorders are identical. If there are constitutional and hereditary factors in this condition we know very little about them, and therefore about the underlying physiology. Miles and Cobb prefer to regard the effort syndrome group of patients as a mixture of somatic and neurotic types, some at one extreme or the other, others, and these will make up the majority, in the middle. Probably all will agree that there is a certain natural selection in the more clearly differentiated members of the group, those consulting a cardiologist and those consulting a psychiatrist. The authors have drawn up a table of symptoms which are common in patients of both contrasted groups, such as palpitation, fatigue on effort, pain in the chest, nightmares, sweating, apprehension *et cetera*, and show the proportions observed in patients diagnosed as suffering from an anxiety neurosis, and those classed as having neurocirculatory asthenia. There is a close correspondence, but with certain differences. For example, in the former group fatigue is more often unrelated to effort, whereas in the latter effort more usually evokes fatigue. Many of these symptoms emerge in a series of case histories given in this article. They describe the history and condition of patients with diverse states, including somatic types of the effort syndrome, psychogenic types with a very similar end state, compulsion neurosis, hysteria, and depressive states. The patients chosen are predominantly of psycho-neurotic type, but the authors point out that more is really known about them from this aspect than from that of possible physiological maladjustments. It is certainly more helpful to think of disease in terms of responses to stimuli, and to do this we need not only understanding of the stimuli, and a clear description of the response, but also some knowledge of the mechanism producing the response and any inhibitions or obstructions hindering its production. There do not appear to be qualitative differences in the physiological system concerned, though quantitative differences have been found. Evidences of instability in the operation of these systems have also been clearly demonstrated, but the causes of such instability are not so clear. That they may lead eventually to organic

¹ *The New England Journal of Medicine*, November 8, 1951.

changes is known in certain other types of psychosomatic disease. Some writers think that there is an underlying constitutional inferiority in the subjects of effort syndrome, and have even suggested that functional general and coronary insufficiency exists in the circulatory system of such persons, but all would not agree that this is proven.

Miles and Cobb, in warning their readers of the uncertainties of anthropological research in these problems, quote Mishkin, who bluntly said: "Give a man a measuring rod and he will beat his brains out." And now where do we stand? No doubt there are extreme prototypes of those patients who can be classified as suffering from either anxiety neurosis or effort syndrome, and it seems fair to admit that a mere list of symptoms will probably drag patients with varying conditions into one net. Miles and Cobb urge that those who approach this disordered state from the somatic or physiological point of view should be aware that mere similarity of symptoms does not justify an assumption that aetiology and psychodynamic make-up are the same in different patients. In conclusion it may be remarked that if a given patient suffering from the effort syndrome is treated after an invariable routine the therapeutic result may not be good. We know that treatment of a relevant psychiatric basis may require much time and patience, but insistence on the somatic factors is likely to do the patient a disservice.

THE USE OF PROCAINE AMIDE IN CARDIAC ARRHYTHMIAS.

PROCAINE, a digitalis-like drug, has been known for nearly fifty years, and has been used to reduce the irritability of the myocardium and the excitability of the cardiac nerves. It prolongs the refractory period, a useful property in the control of the arrhythmias, but it also lowers the blood pressure, and has some tendency to cause convulsive attacks by reason of its action on the central nervous system. The hydrochloride, which has been used till recently, had rather fleeting effects, owing to its rapid hydrolysis in the blood and the formation of an acetyl form in the liver. Introduction of an amide has made a more persistent form of the drug available, which may be administered orally with therapeutic effect. J. Murray Kinsman, W. Reeve Hansen and Robert L. McClendon, having regard to these facts, have carried out an investigation of its properties, and tried to estimate the indications for its use and its risk.¹ In this inquiry only the intravenous route was employed, which is, of course, the most reliable for complete and rapid absorption, and is that performed during anaesthesia, when its most important indications arise. The preparation used was "Pronestyl", in doses of 1000 milligrammes, administered undiluted usually at a rate of 100 milligrammes per minute, but never faster than 200 milligrammes per minute. Frequent blood pressure readings were taken throughout the entire period of observation, and practically continuous electrocardiograms were prepared during the injection and for some time afterwards. Kinsman and his colleagues have recorded the results in all important types of cardiac arrhythmia, as observed in 41 patients with irregularities of the heart, and 11 individuals with normal sinus rhythm.

The effect on the supraventricular types of irregularities was equivocal. No effect whatever was observed in patients with chronic auricular fibrillation, even with doses up to 1000 milligrammes, but one-third to one-half of this dose instantly restored the normal sinus rhythm in paroxysmal fibrillation. Auricular flutter was not affected at all, but auricular ectopic beats were abolished in three patients out of four. Arrhythmias of ventricular origin were much more consistently relieved. Twelve out of fourteen patients with ventricular ectopic beats regained regularity after doses ranging from 200 to 1000 milligrammes, but the irregularity almost always recurred after minutes, hours or days. Even a maintenance dose given by mouth would not control them permanently. Ventricular tachycardia is more important, by reason of its much more serious sig-

nificance. Two of the patients with this condition who were treated had suffered a quite recent myocardial infarction, and they died soon after the injection. In the other two patients the tachycardia stopped promptly after a dose not exceeding 550 milligrammes. Toxic effects were noted, both of subjective and of objective kind. Very few patients had troublesome sensations if conscious; the chief symptoms were flushing of the face, slight giddiness or nausea, and one had some substernal discomfort, but in no instance were the sensations other than slight. However, some objective change was frequently observed. The heart rate altered hardly at all, but the blood pressure practically always fell, the average systolic drop being 32 millimetres of mercury. The degree of fall in the blood pressure appeared to be related to the speed of administration of the dose rather than its size, and its duration was seldom longer than fifteen to twenty minutes. The most striking change in the electrocardiogram was an almost invariable prolongation of the QRS interval, but some flattening or other anomaly of the T waves and interference with sinus regulation were also seen. In order to investigate these effects further the same team carried out a series of observations on the haemodynamic effects on the heart following administration of the drug. Ten patients were studied by cardiac catheterization; they were either healthy with regard to the heart and vascular system, or had controlled and, at the time, symptomless cardiac diseases. Procaine amide was administered to them, after which the cardiac output usually fell, the pulmonary vascular flow decreased and the mean arterial blood pressure fell, with slowing of the blood flow. Mean circulation times were found to be affected, as judged by the appearance of dye. As might be expected, these changes were most evident in patients with diseased hearts. The conclusions drawn by the authors from this work are that the drug is limited in its anti-arrhythmic action, that it has definite objective toxic effects, though these are not serious, and that it should be administered slowly to obviate these effects. They consider that in patients with paroxysmal rapid heart action it should be used only for those whose lives are threatened, or in whom oral administration has failed, and for patients under anaesthesia. Its use in the presence of the correct indications during anaesthesia is validated by pharmacological knowledge.

CANCER AND THE DOCTOR-PATIENT.

Most doctors are alive to the importance of early diagnosis and treatment of cancer and will support heartily any plan to educate their patients on the need for prompt investigation of suspicious symptoms. However, according to evidence produced by B. F. Byrd,² at least some doctors have one rule for their patients and another for themselves. A study was made of doctors admitted to two large metropolitan hospitals in Tennessee suffering from neoplastic disease—a total of 60 between 1925 and 1950. The majority came from the general practitioner group. The four predominant sites of the neoplasms (37 out of the 60 cases), in order of frequency, were the prostate, the upper part of the intestinal tract, the large bowel and the lungs. Of the 37 patients in these groups only seven had primary lesions without either extension to the regional lymph nodes or distant metastases; in only five of the 37 cases were curative procedures carried out, and in 13 cases the condition was classed as inoperable when the patient first came into hospital. Byrd offers two possible explanations: a higher incidence of cancer among doctors than in the general population, which is improbable; neglect by doctors of their own disorders, which seems likely. Further analysis of the time lag between the appearance of clearly suggestive symptoms and the initiation of diagnostic measures reveals extraordinary delay in many cases; as a notable example, no doctor-patient with large bowel neoplasm sought investigation within three months of onset of a characteristic symptom.

¹ *The American Journal of the Medical Sciences*, October, 1951.

Abstracts from Medical Literature.

BACTERIOLOGY AND IMMUNOLOGY.

The Destructive Effect of Traces of Zinc Salts on Complement.

A. E. WILKINSON (*The Journal of Clinical Pathology*, November, 1950) has studied the destructive effect of traces of zinc salts on complement. The inquiry was provoked by the deterioration of a large batch of preserved complement. In a search for the reason, it was found that the particular batch of A.R. sodium chloride yielded a strong reaction for zinc. Parallel tests with other sodium chloride not yielding the zinc reaction showed that the presence of the metal was responsible for the low haemolytic titre of the preserved complement. The presence of serum in tests for complement-fixation lessens but does not abolish the destructive effect of the zinc. The author includes a description of the technique of the test for zinc.

Blood Media for the Cultivation of *Mycobacterium tuberculosis*.

MAURICE S. TARSHIS AND ARTHUR W. FRISCH (*The Journal of Clinical Pathology*, February, 1951) have examined the efficiency of blood media for the cultivation of *Mycobacterium tuberculosis*. They used Bordet-Gengou potato agar base enriched with varying combinations of 5% of glycerin, 25% of egg yolk, and 15% of defibrinated human blood. The control medium was Petragagni's formula or Coper-Cohn egg yolk. Inocula consisted of 3000 or 300 or 30 viable tubercle bacilli H37Rv, as judged by turbidity estimations of dilutions of cultures grown in liquid Tween-Dubos medium. In the medium with defibrinated blood or defibrinated blood with glycerin, the growth appeared earlier by ten or eleven days, and was richer than on any other medium. Small inocula grew particularly well on such media. Aging blood from the blood bank up to fifty-six days proved suitable. The final medium of choice was BG agar base with 1% of glycerin and 25% of bank blood. The authors suggest that the medium may be of use in streptomycin-sensitivity tests.

Non-Specific Shock in Experimental Poliomyelitis.

G. M. FINDLAY AND E. M. HOWARD (*The Journal of Pathology and Bacteriology*, July, 1950) have tested the effect of non-specific shock in experimental poliomyelitis. They used mice in groups of 60, of whom 20 were not infected with virus but had the shock injections, 20 were infected with Lansing virus and then given intravenous injections of "T.A.B." vaccine at varying intervals of time, and 20 received pertussis vaccine, diphtheria toxoid or combinations of these two. None of the control non-infected mice died. In the virus-infected group, the interval between the non-specific shock injection and the onset of paralysis and death of the animal was significantly shorter than in the infected uninjected

controls. The mode of action of the non-specific stimulus is unknown, but the authors postulate an alteration in the metabolism of the nerve supplying the inoculation area, leading to the liberation of nucleotides, which could be used by virus particles encouraging their rate of multiplication. The findings are discussed in relation to paralysis in poliomyelitis in human patients subjected to similar non-specific stimuli; the earlier onset is noted in such circumstances.

Somatic Antigens Isolated from *Bacterium coli*.

LILA HAYES AND N. F. STANLEY (*The Australian Journal of Experimental Biology and Medical Science*, March, 1950) have studied the preparation and properties of somatic antigens isolated from *Bacterium coli*. They were interested chiefly in the polysaccharide complexes which appeared to have some properties in common with polysaccharides from *Salmonella* and *Shigella*, although cross-agglutination tests showed no antigenic relationships to *Salmonella* types commonly isolated in the same laboratory. They used two methods of obtaining polysaccharides: one by mechanical disintegration of dried heat-killed cells (M), the other by the addition of glycine to a thick saliva suspension of young organisms which had not been dried (G). In both the later stage of alcohol and chloroform-amyl alcohol treatment was the same. Both substances dissolved in warm water and gave a colour with the Molisch reagent and none with the biuret. The result of Bial's test for pentose was positive, and that of Dische's test for desoxyribonucleic acid was negative. The substances were toxic to normal rabbits, producing prostration and diarrhoea with death in eighteen hours; the leucocyte count fell and the blood sugar level rose. Rabbits were immunized with a vaccine of the whole *Bacterium coli*, and later given intravenous doses of the polysaccharide; a similar reaction was produced, but to a less degree. Fraction M was antigenic, and rabbit antisera prepared against it agglutinated the strain of *Bacterium coli* from which it was prepared to a titre of 1:5120. Red cells, coated with the polysaccharide and exposed to varying dilutions of its antiserum, were agglutinated in 1:1280 dilution. The two fractions, although mainly polysaccharide in nature, were not identical, and the authors believe that differences in the age of organisms used as well as the different primary treatment were responsible. Finally they have compared their results with those obtained by other workers using *Salmonella* and *Shigella* organisms.

A Plasma Factor Responsible for Hypersensitivity in Vitro of Tuberculin Type.

J. M. MILLER AND C. B. FAVOUR (*The Journal of Experimental Medicine*, January, 1951) have investigated the lymphocytic origin of a plasma factor responsible for hypersensitivity in vitro of tuberculin type. This investigation developed from the observation that white cells from a non-tuberculous subject, if sensitized with tuberculin and exposed to plasma from tuberculous subjects, undergo lysis. Guinea-pigs, immunized with two doses of heat-killed tubercle bacilli and reacting to a

given amount of purified protein derivative, and normal control animals were studied. Human tuberculosis subjects whose plasma could be shown to exhibit this property and normal humans also were used. The authors state that washed leucocytes are not affected by tuberculin as quickly as when they are contained in their own plasma, but after a period of three hours lysis becomes rapid. If normal cells are suspended in tuberculous plasma and tuberculin is added, rapid lysis occurs, and normal plasma can be used to effect lysis of further normal cells if it has previously been in contact with tuberculous cells. Precipitation of euglobulins from normal plasma into which the factor has been released from tuberculous leucocytes shows the factor to be contained in the euglobulin fraction. Suspensions of lymphocytes will shed the plasma factor, but suspensions of neutrophile cells will not.

The Role of Some Higher Peptides in Inflammation.

W. G. SPECTOR (*The Journal of Pathology and Bacteriology*, January, 1951) has studied the role of some higher peptides in inflammation, in an attempt to find whether the previously observed capacity of a tryptic digest of blood albumin to increase permeability of capillaries and cause emigration of leucocytes was a biological property of a single substance or of a group of compounds. He used the rat as the test animal, trypan blue in saline injected intravenously as the indicator of increased permeability, and the shaved skin of the abdomen as the site on which test solutions were injected. Readings were made by a colleague who had no information as to which inocula were controls and which test fluids. Leucocytic emigration was tested for in a similar fashion except that no dye was injected, and the animal was killed and the area of skin excised and examined histologically for leucocytic increase and change in distribution. Peptic digests of fibrin were prepared and purified by a number of different chemical processes before being tested and analysed. They were all fractions salted out by 75% saturation with ammonium sulphate and had a surface activity. The chain length of the peptide fractions appeared to have 8-14 amino acid residues. In experimental burns of the rat skin, the immediate increase in permeability seemed too fast for the enzymic breakdown necessary to produce such peptides; the author comments that there must be some mechanism for their liberation at the site of tissue injury, where they produce some of the changes of acute inflammation.

Antibiotic Sensitivity Tests Against *Escherichia coli* III B.

W. W. FERGUSON, J. C. JENNINGS AND R. Y. GOTTSALL (*The American Journal of Hygiene*, May, 1951) have performed in-vitro sensitivity tests with eight antibiotics against *Escherichia coli* III B, a special type of coliform bacillus associated with infant diarrhea. They state that the organism rarely occurs in normal infant and adult stools, it decreases during the convalescence of patients harbouring it, and an agglutinin titre to it can be found in the patient's serum, so that evidence is accumulating to suggest that its relationship to diarrhoeal disease is

protein of animals. Substances shown to be normal by the authors are not quickly absorbed from their own solution of three per cent. If normal tuberculous fluid, rapid absorption can occur normally. In contact with plasma into which it is released, shows the globulin antibodies but suspended will not.

Peptides

of Pathology, 1951) the higher attempt observed of blood supply of the group of as the alkaline indicator and the site injected. Colleague to which such test was made except the skin usually for in disease were number before they were saturated and had lengthened to s. In the skin, breakable perhaps there their injury, of the

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more than casual. Thirty-two strains of the organism were tested. Variability in the fermentation of salicin is associated with a variation in sensitivity to streptomycin. The fermenters were sensitive, and the non-fermenters uniformly resistant. The sensitivity to penicillin was not incorporated in the table, but the text mentions 50 units per millilitre as the lowest concentration inhibiting growth, and 100 units were required for all other strains tested. The inhibitory level of "Chloromycetin" was 6.3 to 12.5 microgrammes per millilitre. Aureomycin was generally effective at 3.2 microgrammes per millilitre, terramycin at 12.5, neomycin at 1.8. A single strain was uniformly sensitive to lower concentrations of all drugs in the order of one-fourth the amount. The authors conclude that aureomycin appeared the most effective drug under the conditions of the test.

HYGIENE.

Plant Feeding Programme.

M. ZEALAND, M. SENA AND O. SUSSMAN (*American Journal of Public Health and The Nation's Health*, July, 1951) consider that industrial firms do not take sufficient interest in their employees' nutritional problems, and that there is a loss in the productive capacity of workers through lack of understanding of the relationship between nutrition, health, morale, fatigue, and industrial diseases. They have surveyed the methods of supplying food to workers in industry in New York and found five common methods in use: cafeterias or lunchrooms with attached kitchens were owned and controlled by the management; similar facilities were owned by the management, but operated by the workmen's representatives; similar facilities were owned by the management, but leased to people not connected with the firm; food was delivered to the factory by a food preparation organization outside the factory; lunch was prepared at home and taken to the factory by the workman. It was often found that the persons employed by management in cafeterias and lunchrooms were not trained and that they were those who had failed as efficient workers in other parts of the factory. The same applied where the control was in the hands of the employees' representatives. Where the lunchrooms and cafeterias were leased to some outside firm it was found that often no interest was taken in the preparation of nutritious meals, and in addition health hazards were often associated with the preparation of the food. Where prepared meals were delivered to the factory it was often found that their preparation was unsatisfactory. When the workman brought his own lunch from home he was the only one affected if his lunch had been improperly prepared, or if it did not contain the required ingredients for a nutritious meal. The authors have made the following recommendations to improve the conditions found during their survey: (i) that the management must cooperate with the medical and cafeteria staff to ensure that well-balanced nutritious meals are available for their employees; (ii) that persons employed in the preparation of food should be trained in the principles of sanitation, food-handling, nutrition

and bacteriology, in so far as they relate to food preparations; (iii) that the employees should be trained to recognize and demand good nutritious meals; (iv) that periodical medical examinations should be made of employees by the factory medical department for nutritional deficiencies.

A Punch-Card Code for the Classification of Pulmonary Tuberculosis.

B. PAPANICOLAOU (*Acta tuberculosea Scandinavica*, 1951, Volume XXV, page 256) proposes a five-digit code which makes possible a fairly complete descriptive classification of pulmonary tuberculosis. Two selected features for each of five categories have been arranged in a pattern. Each feature is assigned a digit from 0 to 9 in ascending order of seriousness. The first of the five categories relates to the excretion of tubercle bacilli, the second to the type and form of tuberculosis, the third to the situation of the lesions, the fourth to the presence of cavities and effusions, and the fifth to clinical status and symptomatology. The code after having been approved by a committee of the Greek Ministry of Hygiene has been recommended to the World Health Organization.

Arsenic and Cancer.

L. S. SNEGIREFF AND O. M. LOMBARD (*Archives of Industrial Hygiene and Occupational Medicine*, September, 1951) refer to the almost universal presence of arsenic on the earth's surface and the almost universal association of the human race with arsenic in some of its forms. In their investigation into the relationship between arsenic and cancer they collected data from medical records, personnel files, death records and other available records regarding persons who had worked in metallurgical industries involving exposure to arsenic compounds over a period of many years. In their study of Plant A, where large amounts of arsenic trioxide were handled, they found a slightly higher proportionate mortality from cancer among the employees than in the State-adjusted figures. But the same was found true of Plant Z, where arsenic was not handled, but where the other factors were comparable. Statistical tests showed that these differences were chance fluctuations and not significant. The authors conclude that on the evidence examined the handling of arsenic trioxide in the industry studied did not produce a significant change in the cancer mortality of the employees, and that other factors in addition to arsenic must be considered significant in the causal relationship to cancer.

The Hazard of Acquiring Tuberculosis in the Laboratory.

E. LONG (*American Journal of Public Health and The Nation's Health*, July, 1951) discusses the infection of laboratory workers with tuberculosis from four points of view: portals of entry, frequency of different types, treatment and prognosis, and prevention of infection. He states that the skin, eye, alimentary tract and respiratory tract may serve as portals of entry for accidental laboratory infection with tubercle bacilli. Exact information is lacking on the relative frequency of laboratory infection through these portals of entry. The source of skin

infection is usually known, but proof of the origin of alimentary and pulmonary infections is difficult. More often than not, pulmonary infections in laboratory workers are assumed rather than demonstrated to be of laboratory origin. Scientifically trained investigators appear to be more frequently infected than assistants, but further study, based on the numbers of persons at risk, is necessary to furnish exact information. The treatment of pulmonary tuberculosis acquired in the laboratory is like that of pulmonary tuberculosis acquired in any other manner. The treatment of skin tuberculosis depends on individual circumstances; the present tendency is to employ both surgical measures and chemotherapy. Measures to prevent laboratory infection with tubercle bacilli must be in effect at all times in laboratories engaged in the study and diagnosis of tuberculosis. The most important consideration is perfection in laboratory technique. Appropriate rules of procedure have been drawn up. B.C.G. vaccination of tuberculin-negative personnel is recommended as an adjunct to other measures. Periodic tuberculin testing is essential if vaccination is not practised. X-ray examination of all personnel must be carried out at intervals not to exceed six months.

Control of Dusts by Water Mists.

K. W. NELSON (*Archives of Industrial Hygiene and Occupational Medicine*, July, 1951) discusses the use of water in various forms in the suppression of industrial dusts. Laboratory and field trials are described in which the use of water mists reduced the dust concentrations by 50% to 60%. Air-borne dust particles are wetted and are deposited by impingement on a surrounding surface or, because of the increased particle size, settle near the source instead of being widely dispersed. Crushed material passing through the zone of concentrated mist is surface-moistened, but not over-wetted, and is less dusty in later stages of handling. Commercially available pneumatic atomizing nozzles are used to produce water mists in the laboratory and in the field. Water and air are mixed internally to produce a round, a wide-angle round, or a flat spray pattern. Atomization is complete if the pressures are correct. Measurements indicate that the droplets range in size from about 10 μ to 50 μ in diameter, the majority being less than 25 μ . A typical nozzle which produces a good volume of mist for dust suppression uses, according to the manufacturer, 10.8 gallons of water per hour and 5.3 cubic feet of free air per minute when water is supplied at 40 pounds to the square inch and air at 50 pounds to the square inch. The author considers that dust control with water mists has the advantage of low costs and simple installation. It does not control dusts in the sense that a well-designed exhaust ventilation system does, but it may be useful as another mode of attack on dust problems. Applications suggested are alleviation of dust problems which are temporary and would not warrant construction of a complete ventilation system, control of nuisance dusts, and control of pneumoconiosis-producing or toxic dusts in situations where the degree of control attainable by mists would reduce the concentration to satisfactory levels.

Special Articles for the Clinician.

(CONTRIBUTED BY REQUEST.)

XIV.

HEMATEMESIS.

THE treatment of haematemesis and melena has been and still continues to be a cause of much difference of opinion and debate. Opinions of a widely different character, accompanied and supported by masses of statistics, have been expressed, particularly in connexion with the indications for surgical intervention, the timing and rapidity of blood transfusion, and the degree to which the blood lost should be replaced.

Meulengracht (1948) reports 1031 patients suffering from bleeding ulcer treated by liberal feeding and transfusion with only 26 deaths (2.5%). In all the fatal cases the patients were over forty years of age and many had large ulcers penetrating the pancreas or liver or had associated complicating diseases. Although previously he had not advocated surgical treatment to control haemorrhage, Meulengracht states that he will in future consider surgery for patients over forty years of age with persistent or repeated haematemesis and threatening to die in spite of repeated blood transfusions.

C. D. Needham and J. A. McConachie (1950) record 476 consecutive cases of haematemesis and/or melena with a mortality rate of 13.9%. Operation was undertaken after severe and prolonged bleeding in eleven cases with seven deaths; in four there was associated pyloric stenosis and in one perforation was present; all of these were fatal. They concluded that: "Recurrent hemorrhage after admission to hospital was the most reliable warning of the serious nature of the bleeding in all age groups, the risk of dying being 8 to 10 times greater in the recurrent group. An eroded artery in the base of an ulcer is usually the source of this type of haemorrhage."

G. Gordon Taylor (1946) found that the mortality from haematemesis of proved ulcer origin was 24%. When he began, in 1933, to operate on these patients, the death rate among those so treated within twenty-four hours of the onset of the bleeding was 5%. Of eleven patients operated on late, five died.

F. Avery Jones (1947) records 687 patients with a mortality of 8%. During the first 400 admissions surgery was undertaken in three cases as a last desperate measure and all three patients died. As a result of the experience gained in these cases, it was decided to undertake surgery in those patients, particularly over fifty, with good clinical evidence of a chronic ulcer who were free from medical complications, and who had a brisk recurrent haemorrhage after admission to hospital. Seven patients were operated on with one death. He found that recurrent bleeding in chronic ulcers, particularly if gastric, carried a very high mortality with medical treatment, but that in acute ulcers with recurrent bleeding the mortality was very low. Old age, large chronic ulcers, and associated medical complications were important factors in contributing to death.

The wide variation in mortality in the several series of cases just quoted can hardly be due entirely to the methods of treatment employed, but is almost certainly due, at least in part, to difference in type of the ulcer and the presence or absence of associated complications.

In any complex problem, in which there are many factors which have a material bearing on the course and outcome of the condition, statistical evidence is bound to be misleading and any attempt to lay down hard and fast rules as to what course of action should be taken is not likely to be successful.

It is frequently stated, for example, that a brisk recurrent haemorrhage after admission to hospital is an indication for immediate operation. This is almost certainly true if the patient has a chronic ulcer and there are no serious medical complications, but recurrent bleeding is not uncommon in acute ulcers in which the medical mortality is very low. If operation was undertaken as a routine in such cases the surgeon would probably fail to find an ulcer, and would then have to perform a blind gastrectomy or else close the abdomen, and there are advocates for both these courses of action. Unless surgical anaesthetic and medical skill of a very high order is available, the surgical mortality might well be higher than if medical treatment was persisted with.

This does not necessarily mean that there may not be patients with acute ulceration, even young people, who will bleed to death under the best of medical care, and may be saved by timely and expert surgical intervention. The problem, admittedly a very difficult and at times almost an insoluble one, is to preselect those patients whilst there is yet time. In no other condition in the whole range of medicine is the old adage so true: "Nine-tenths of wisdom is being wise in time."

The making of a decision as to what should or should not be done to a patient suffering from haematemesis and/or melena is essentially an individual one, and should be made only after a very careful and honest consideration of all the factors concerned, and what is just as important is the placing of them in their proper perspective.

Some of the essential factors may be difficult or impossible of decision, for example, whether the patient has an acute or chronic ulcer or whether the bleeding is due to some other lesion. Nevertheless the attempt should be made, and made at once, for there is one thing on which there is fairly general agreement, that late operation on a patient who has had many transfusions carries a very high mortality even if he arrives on the operating table with a haemoglobin percentage of 90.

The first problem is to exclude, as far as is possible, causes other than peptic ulcer.

Approximately 90% of cases of bleeding from the upper part of the gastro-intestinal tract are due to chronic ulcer, acute ulcer, or some form of haemorrhagic gastritis.

In the Avery Jones series of 687 admissions, 363 were due to chronic ulcer, 252 to the "acute lesion group" and the remainder to various causes, the commonest of which were malignant disease, cirrhosis of the liver and Banti's disease.

Other rarer causes are simple tumour of the stomach or intestine, ulceration in a Meckel's diverticulum, localized arteriosclerosis of gastric vessels, hereditary telangiectasia, carcinoma of the ampulla of Vater and blood disorders such as thrombocytopenic purpura and acute leucæmia.

A careful history should be taken and a full clinical examination made particularly with reference to peptic ulcer, carcinoma of the stomach and cirrhosis of the liver. Cirrhosis and ulcer may coexist, as in one patient whose abdomen was explored for repeated haematemesis and a gross cirrhosis of the liver was demonstrated. Post-mortem examination disclosed a large chronic gastric ulcer which was the source of the bleeding.

Particular attention should be directed to the presence of any enlargement of the spleen, any signs of portal cirrhosis or hypertension, or evidence of a general bleeding tendency which would suggest that the bleeding was primarily due to some extragastric cause.

In some cases the cause of the bleeding remains obscure, even after prolonged observation of the patient and intensive investigation, including exploratory laparotomy.

I. R. Jankleson (1951) found that about 5% of cases remained undiagnosed even after several episodes of severe bleeding. He followed 27 such patients for periods of two to twelve years. In 16 cases the cause of the bleeding was not discovered, and in 11 in which a diagnosis was ultimately made the causes were as follows: hypertrophic gastritis, 2; gastric ulcer, 2; duodenal ulcer, 2; haemangioma of the duodenum, 1; hiatus hernia, 1; cancer of the stomach, 1; cancer of the liver, 1; and cirrhosis of the liver, 1. In some of these cases surgical exploration may be the only means of arriving at a diagnosis and this is recommended after repeated episodes of bleeding.

It would seem that approximately 90% of cases of bleeding from the upper part of the gastro-intestinal tract are due to acute or chronic lesions of the ulcer type, and of the remainder about 5% can be shown to be due to other causes, whilst a small percentage remain obscure even after prolonged observation and investigation.

It would be reasonable therefore, if causes other than ulcer and gastritis are excluded as far as is humanly possible, to assume for purposes of treatment that an ulcer is present.

If it is decided that an ulcer is present, what are the factors that should be carefully weighed and considered before planning a course of treatment? These will be briefly considered in turn.

1. The first problem, and this is of major importance, is to decide if possible the site of the ulcer, and whether it is acute or chronic. Post-mortem records show that, although death may occur from acute ulcer, the majority of fatalities are due to haemorrhage from an open artery at the base of a chronic ulcer. The mortality from bleeding from a chronic

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ulcer, particularly if it is recurrent, is very high (about 50% in recurrent bleeding from a chronic gastric ulcer and about 30% in recurrent bleeding from a chronic duodenal ulcer). In acute ulcers, however, the mortality from haemorrhage, even if it is recurrent, is very low.

It is important therefore to determine if possible whether the ulcer is acute or chronic. This decision may be easy; in some cases it can be made with a high degree of probability and in others it may be impossible.

Experience shows that the mere length of the history, the site of the pain and its food relationship, and even the severity of the haemorrhage are unreliable in deciding the nature of the ulcer. An acute ulcer may have a long history and a chronic ulcer may first manifest itself by a sudden haemorrhage.

The most reliable criteria of a chronic ulcer are as follows: (a) previous X-ray evidence of a chronic ulcer; (b) a history of bouts of dyspepsia of an ulcer type lasting for months and not days or two or three weeks, as is usual in a recurring acute ulcer; (c) the persistence of pain which has resisted efficient medical treatment; (d) presence of pain in the back; (e) presence of recent pain, particularly if severe and lasting more than three weeks; (f) recurrence of bleeding after the third day or very severe haemorrhage—both favour chronic ulcer. Chronic ulcers are also relatively much more common in males.

2. The majority of deaths occur over the age of forty-five years, probably owing to the presence of degenerative arterial changes. Nevertheless, patients much younger die of haemorrhage, and the youth of the patient should not debar him from the benefits of surgery, particularly if it is known that a chronic ulcer is present and haemorrhage has recurred within a few days of the first bleeding.

3. The patient should be carefully examined for medical complications such as pneumonia, cirrhosis of the liver and chronic nephritis. In many of the fatal cases, complications other than those connected with the ulcer have contributed to the fatal issue.

4. Death rarely occurs in the first bleeding or at any rate in the first day or two, but usually occurs after several brisk recurrent haemorrhages. Occasionally, however, death may occur from a rapid and severe haemorrhage from the erosion of a large artery.

5. Gastric surgery has progressed very much even in the past few years.

Robert S. Lawson (1945), in reviewing the results of operation for peptic ulcer at the Royal Melbourne Hospital over a ten-year period from 1927 to 1937, found that the mortality for elective partial gastrectomy was 30%.

Grayton Brown (1951) records 60 cases of subtotal gastrectomy with only one death.

From 1947 to 1950, 241 elective subtotal gastrectomies were performed at the Royal Melbourne Hospital with a mortality rate of 4.6%. This marked lessening in operative mortality will naturally influence the physician in seeking surgical help much earlier and more frequently than he would have done only a few years ago. It is hardly necessary to mention that in making a decision whether surgical treatment should be invoked, the degree of surgical anaesthetic and post-operative medical skill available may quite well be a deciding factor.

6. The difficulty of locating even chronic ulcers by palpation and inspection of the stomach and duodenum has been emphasized by Wright Smith (1937). In reviewing 218 cases investigated at autopsy, he found 62 in which haemorrhage was the main factor causing the patient's death. It is important to notice that 42 of these ulcers were gastric and 20 duodenal. All the duodenal ulcers were chronic, and of the gastric ulcers 36 were chronic, one was subacute and five were acute; thus is emphasized the great preponderance of chronic ulcers in fatal haemorrhage. All except four of the ulcers were in the duodenum or near the gastric pathway in the lower half of the stomach. This would seem to support the contention of those who advise that if the abdomen is opened to stop bleeding and no ulcer is found, gastrectomy should be performed.

7. Post-mortem records show that in some of the fatal cases there has been no bleeding for several days. Death has been due to shock, dehydration and anoxæmia affecting vital organs and causing irreversible changes. In most of these the blood urea level has been greatly elevated. This indicates the necessity for continually keeping the haemoglobin at a safe level and preventing dehydration. There is much difference of opinion as to what constitutes a safe level, some placing it as low as 40% and others as high as

80%. Probably 60% to 65% is a reasonably safe level, which can easily be increased if operation is contemplated.

After this consideration of the various factors which influence the prognosis of gastro-duodenal haemorrhage, the management of the different clinical types, as presented for the first time for a consultant opinion, will be briefly discussed.

1. It is often said that a little blood makes a big show, but this is not the case when a patient with a duodenal, or occasionally a gastric ulcer, bleeds freely but does not vomit blood. If the tarry or occasionally red coloured motions are not noticed, the diagnosis may be missed.

The patient usually looks pale, and depending on the amount of blood lost, may or may not be shocked and present the usual features of acute blood loss. The pulse may be rapid and the blood pressure low. Precordial distress with tightness and pain, due to myocardial ischaemia and occasionally to an actual coronary thrombosis precipitated by the haemorrhage, may be present. Even in those patients without a coronary thrombosis, marked cardiographic abnormalities are frequently seen with depression of S-T segments and poor T waves. A day or two after the onset there may be some rise in temperature. A diagnosis of acute heart failure of influenzal or viral origin, coronary thrombosis, acute colitis or acute bleeding from the large bowel may be made. The patient's appearance should suggest that he has lost blood. A finger inserted into the rectum will usually recover a small portion of tarry stool, and on questioning the patient a history of ulcer dyspepsia can often be obtained.

2. The patient when first examined may have severe anaemia with a haemoglobin value in the region of 30%, but no evidence of shock or dehydration. The blood pressure may be normal and the pulse slow in rate and of good volume. There have probably been small bleedings at intervals during the previous few weeks or months. A slow drip transfusion, with packed corpuscles if there is any evidence of venous engorgement, will enable the haemoglobin to be restored to a satisfactory figure.

These patients usually give no trouble with recurrent bleeding while in hospital. The decision as to the necessity or otherwise for surgical treatment can be deferred until full investigation has been made to determine the site and the nature of the lesion causing the haemorrhage.

3. The patient is examined immediately after or during the haemorrhage. He is not shocked and the haemoglobin value does not fall below 60%.

Even after a moderately severe haemorrhage the patient's appearance on admission to hospital may be misleading, and it is advisable to assess his condition in an hour or two, when, after rest and an injection of morphine, his general condition and colour may be greatly improved. Initial haemoglobin readings may also be misleading if taken before there has been time for haemodilution to take place.

The patient should be watched carefully, and hourly or half-hourly readings taken of the pulse and blood pressure. The initial treatment is medical.

If the haemoglobin value does not fall below 60% and the patient is not shocked, medical treatment should be continued, and even transfusion is unnecessary.

If the haemoglobin value falls below 60%, and certainly if it falls below 50%, transfusion should be undertaken. If the patient's general condition remains good and there is no difficulty in maintaining a satisfactory blood pressure and haemoglobin level, medical treatment is continued.

Shortly after admission to hospital the patient may have a brisk recurrent haemorrhage. The underlying lesion may be either a chronic gastric or a duodenal ulcer, in both of which the mortality from continuation of medical treatment is very high (about 50% in the former and 30% in the latter), or an acute ulcer in which the medical mortality is comparatively low (about 9%).

If it is decided that the patient has a chronic ulcer and particularly if it is gastric, operation is advisable, provided there are no contraindicating medical complications and expert surgical and anaesthetic skill is available.

If after careful consideration of all the available evidence it is not possible to make a probable diagnosis of a chronic ulcer, then it is much more difficult to decide whether or not to continue with medical treatment.

Some surgeons advise operation on all these patients, although they disagree as to what should be done if no lesion is discovered. In this event some would advise closure of the abdomen, whilst others would perform a "blind" gastrectomy.

It is in this group that further study is very desirable in order to obtain a more rational foundation on which to base sound therapy. Early gastroscopy and X-ray examination have been advised, and even practised, but so far have not gained general acceptance.

Avery Jones (1947) has shown that brisk recurrent haemorrhage from an acute lesion usually takes place within the first two days. Among 40 patients with acute lesions 11 had brisk recurrent haemorrhage and all but one of these haemorrhages took place within two days of onset. He considers that recurrence of haemorrhage after the third day suggests a chronic ulcer.

Thus it would appear to be reasonable to operate on those patients in whom the nature of the lesion is uncertain if a brisk recurrent haemorrhage takes place after the third day provided the patient is "good risk" over forty-five years of age and expert surgical and anaesthetic facilities are available. This question is still a very open one and nobody should suffer reproach if medical treatment is continued.

4. The patient is first examined with severe haemorrhage and presenting the usual features of severe blood loss—collapse, pallor, sweating, air-hunger, low blood pressure and elevated pulse rate. There may not have been time for haemodilution to occur and the haemoglobin value may still be high and give a false indication as to the necessity for emergency transfusion. Most, but not all, of these cases are due to bleeding from an open artery in the base of a chronic ulcer.

Oxygen and sufficient morphine to allay restlessness and anxiety should be given and a transfusion of at least two litres of blood within one or two hours. In most cases the patient will respond and he should then be watched for any further recurrence of bleeding. If, however, he fails to respond satisfactorily and it is difficult to maintain a satisfactory blood pressure and haemoglobin level, further transfusion should be given and the patient submitted to operation.

5. A haemorrhage sometimes occurs while the patient is undergoing full medical treatment in hospital for a chronic ulcer. The mortality, if medical treatment is continued, is high. The site of the ulcer is usually known. Unless there are contraindicating medical complications, the patient should be prepared for operation if proper facilities are available.

6. The patient may be examined after many recurrences of bleeding, having been given transfusions each time and then suffered further haemorrhage. In most of these a chronic ulcer is present. The mortality will be high whether operation be undertaken or not. The patient is not as good a surgical "risk" as he appears to be, and this should be taken into account in considering the advisability of operation.

If the site of the ulcer is known, and particularly if it is in the stomach and easily accessible, it is probably better to operate if the patient still appears to be a reasonable surgical "risk", even though it is known that the mortality will be high. It will probably be greater if medical treatment is persisted with. A few of these patients may be saved by expert surgical intervention.

The Medical Management of a Bleeding Ulcer.

The most important advances in the medical management of the bleeding ulcer in recent years have been the introduction of drip transfusion by Marriott and Kekwick and early and liberal feeding by Meulengracht.

The patient should be kept at rest in bed, reassured, and given an injection of morphine to allay his restlessness and anxiety. Subsequent sedation may be achieved by regular administration of sodium phenobarbital one grain by injection every four to six hours, reinforced if necessary by an occasional injection of morphine. Over-sedation should be avoided.

The blood pressure and pulse rate should be recorded every hour, or in some cases every half-hour, and blood taken for typing and estimation of blood urea content and haemoglobin and hematocrit values.

The patient's condition on admission to hospital may be misleading, and unless he is obviously shocked and in need of an emergency blood transfusion, it is advisable, provided he is carefully watched, to give an injection of morphine, and assess his condition an hour or two later. The initial haemoglobin value may also give an unduly high reading if estimated before there has been time for haemodilution to occur.

The indications for transfusion have already been discussed, the main objects being alleviation of shock, pre-

vention of death from exsanguination and the continued maintenance of the haemoglobin at a safe level (about 60% to 65%), so that the patient will not run the risk of damage to vital organs from anoxæmia, will be able to withstand recurrent bleeding without danger to life, and will be kept in a condition suitable for operation should this become necessary.

Feeding by mouth can be commenced at once except for those patients who have had a massive haemorrhage, when it is better delayed for eight to ten hours.

Two-hourly feedings of five or six ounces, made up of the following, may be given: citrated milk, strained oatmeal, arrowroot, cream of wheat, orange juice, tomato juice, soft purée of vegetables or fruit, cream, egg flip, custard, junket, plain jelly, "Benger's Food", or simple pudding with cream. One-third normal saline flavoured with fruit juice can be given in addition to allay thirst.

A simple alkaline powder, to be taken six times daily, may be prescribed, and as soon as the stools have resumed a normal colour, iron, for example, "Colliron", one drachm four times daily, may be given. Ascorbic acid, 100 milligrammes three times daily for the first five or six days and thereafter 50 milligrammes twice daily, may also be of some assistance.

The bowels should be left undisturbed for at least four days or even longer if there is no abdominal distension or discomfort. A simple enema may then be given.

When there has been no bleeding for two or three weeks appropriate investigations should be undertaken to determine if possible the site and nature of the lesion causing the bleeding.

The management of the bleeding peptic ulcer is in most cases on medical lines.

Judicious sedation, early and liberal feeding, prevention of dehydration and transfusions as indicated are the most important points in the treatment.

Some patients will die of haemorrhage if medical treatment is persisted with. Some of these might be saved by timely surgery. This applies particularly to patients over forty-five years of age with a chronic ulcer without grave medical complications who have a brisk recurrent haemorrhage within a few days of admission to hospital.

Late surgical treatment for haemorrhage carries a high mortality, but may in selected cases be life-saving.

L. E. HURLEY,
Melbourne.

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British Medical Association News.

SCIENTIFIC.

A MEETING of the Victorian Branch of the British Medical Association was held at the Children's Hospital, Melbourne, on November 21, 1951. The meeting took the form of a series of clinical demonstrations by members of the medical and surgical staff of the hospital.

Nephritis.

DR. ROBERT SOUTHBY presented a series of patients to illustrate the various types of nephritis occurring in children. The first patient, a boy, aged ten years, had had several teeth extracted ten days before he felt ill and was noticed to be passing red urine. One of the carious teeth was complicated by an alveolar abscess. He was slightly puffy under the eyes, was disinclined for food, and had suffered slight transient headache. The urine contained macroscopic amounts of blood and a little albumin. Microscopically it was found to contain numerous red blood cells, blood casts and cellular casts. The blood pressure was 135 millimetres of mercury, systolic, and 90 millimetres, diastolic. Dr. Southby said that the child's condition was a classical example of acute haemorrhagic or focal nephritis (or Type I). He had remained rather ill for ten or twelve days, after which time he gradually improved, and by the end of the fourth week of his illness the urine was free of blood and albumin, the blood pressure was 90 millimetres of mercury, systolic, and 60 millimetres, diastolic, and microscopically the urine was found to contain only a few red blood cells. Dr. Southby mentioned that in the type of nephritis concerned, which was by far the one most encountered in children, the red blood cells were the first to appear in the urine and the last to disappear before convalescence was complete.

The second patient, a small girl, aged seven years, had a very similar clinical history, but in her case the nephritis was complicating a group of impetiginous lesions on the legs and on one forearm of approximately four weeks' duration. The illness followed an equally satisfactory course, and in six weeks from the onset the child was apparently recovered.

The third child in the group, a boy, aged nine years, had suffered from acute follicular tonsillitis two weeks previously; at that stage it was noticed that he was passing very smoky urine and became very drowsy and confused. He was admitted to hospital in a semi-uremic state with a small amount of oedema of the face and ankles, a diminished urinary output, a blood urea content of 75 milligrammes per 100 millilitres and urine containing red blood cells, cellular and granular casts and a fairly heavy cloud of albumin. After being very ill for five days the patient began to recover quickly, and three weeks after the onset of the illness the urine contained only a trace of albumin and a few red blood cells, and the blood urea content was 26 milligrammes per 100 millilitres. Four weeks later again (on the night of the meeting) the boy appeared to be exceedingly well. Dr. Southby said that the type of nephritis concerned was in most cases associated with a definite source of infection some week or fortnight before the first manifestation of nephritic trouble. The infective agent was almost always a streptococcus, being associated, for example, with tonsillitis or impetigo.

The next patient, a small boy, aged six years, had had almost all the possible clinical features and complications of the subacute type of nephritis (Type II). Two and a half years previously he had been an in-patient with an illness of insidious onset; he had malaise, anorexia and undue fatigue from mild exertion, together with slowly increasing pallor and puffiness of the face, extremities and abdomen. He was very ill on admission to hospital, and the urine was loaded with albumin and contained numerous granular casts, a few of the hyaline variety, and a few red blood cells. There was in addition a severe hypoproteinæmia. After two months, during which the child was seriously ill with generalized oedema including ascites and pleural effusion and gross oedema of the limbs, sacral region and face, he contracted measles; with that illness he staged a dramatic and complete recovery, as a result of which there was profuse diuresis with rapid disappearance of all his oedema, and in addition the urine remained free of albumin for two weeks. The dramatic change was literally "too good to be true", and within another month the boy had an exacerbation accompanying an attack of right basal lobar pneumonia. Having recovered temporarily, he then became very much worse, and the ascites was gross and the abdominal wall extremely tense: at that stage he complained of severe pain in the lower part of the abdomen and his temperature rose suddenly to 103° F. Paracentesis revealed opalescent ascitic fluid; examination of a smear of this showed it to be loaded with Gram-positive encapsulated diplococci, which were proved by culture to be pneumococci. Intensive penicillin and streptomycin therapy was instituted; in a few days there was again a dramatic response, and within ten days the fever had subsided, the fluid from the abdomen was clear again and, what was more, it was sterile on culture. Clinical improvement having been maintained for at least one month, there was a return of fever and abdominal pain, mostly in the suprapubic region, and once the ascitic fluid was turbid and loaded with pneumococci. Again, in desperation,

penicillin and streptomycin therapy was instituted, and once more the miracle occurred; the small child recovered from his second attack of pneumococcal peritonitis, an occurrence which Dr. Southby considered must be unique. During the next six months the patient continued his stormy convalescence and experienced no less than four distinct and severe exacerbations, one with a most intense attack of varicella associated with a hemorrhagic rash, one with a Flexner type of dysenteric infection, the third with bilateral otitis media, and the fourth without any evident intercurrent infection. Early in 1951 there was once more a period of improvement, in which the urine was free of albumin for seven consecutive weeks. At that stage it was advised that a pair of slightly infected tonsils should be removed. That was decided upon, not because the tonsils were regarded as being the specific cause of the original nephritis, but rather with the idea of minimizing the risk of further secondary infection. The operation was successfully negotiated, and apart from transient mild albuminuria for a couple of days after operation, the boy proceeded to improve greatly in his general health; at the time of the meeting (two and a half years after the onset of illness) the patient presented as a very healthy looking, active and alert little boy about to commence schooling. He had had no albuminuria for five months, his blood urea content was 17 milligrammes per 100 millilitres, his haemoglobin value was 100%, his blood pressure was 110 millimetres of mercury, systolic, and 75 millimetres, diastolic, his urine was microscopically clear, and the urea clearance figure was reported as 120% of normal. Dr. Southby considered that the patient had presented practically every clinical sign and complication which might occur with Type II nephritis, and although the boy appeared very well indeed at the present time, Dr. Southby thought that the ultimate prognosis should be still rather guarded.

The fifth patient was a girl, aged eleven years, who had been ill for approximately eighteen months. For several months before her admission to hospital in October, 1950, she had been noticed to have puffiness under the eyes in the mornings, together with languor and progressively increasing pallor. There was an indefinite history of previous throat infections. On her admission to hospital the urine was found to be loaded with albumin, and microscopic examination revealed many cellular casts and numerous red blood cells. At that time the blood urea content was 21 milligrammes per 100 millilitres and the serum protein content was 6.1 grammes per 100 millilitres (the albumin content being 3.1 grammes and the globulin 3.0 grammes per 100 millilitres). The blood pressure reading was 160 millimetres of mercury, systolic, and 110 millimetres, diastolic. The patient had followed a very protracted course in spite of rest and a sustained strictly salt-free diet, and now after at least twelve months of hospital treatment there was a considerable amount of albumin in the urine, with oedema of the legs up to the knees, numerous granular and cellular casts in the urine, and a blood pressure of 160 millimetres of mercury, systolic, and 90 millimetres, diastolic. The blood urea figure had varied from 38 to 54 milligrammes per 100 millilitres. Dr. Southby said that with such a lengthy convalescence and the persistently raised blood pressure in a girl of the patient's age it was felt that the ultimate prognosis must be far from encouraging; perhaps the only clinico-pathological finding in her favour was that the urea clearance figure was reported as 98% of normal.

Dr. Southby finally referred to the child with chronic nephritis who had been admitted to hospital suffering from convulsions due to incipient uræmia—frequently the first indication of any serious illness. He said that such children nearly always had almost water-white urine of low specific gravity (1005 to 1008), the low figure being maintained throughout the twenty-four hours. The urine rarely contained albumin, or perhaps it contained only a faint trace, and microscopic examination showed only a few hyaline casts. Fortunately, such children were not commonly encountered, as the outlook was uniformly hopeless and some did not recover from even the first attack of convulsions. The kidneys in such children were of the small, contracted, granular and very fibrotic type. Sometimes there was a family predisposition to this type of renal disease. Only rarely did the subacute type merge gradually into the true chronic type in children, the former most often terminating as the result of a fatal intercurrent infection.

In concluding his remarks, Dr. Southby mentioned that with the great majority of children presenting with acute haemorrhagic nephritis (and they constituted by far the largest group of nephritic children) the course was short and sharp, and the recovery was generally complete and without later sequelæ. Finally, the clinical manifestations

of the various types were summarized as follows: acute—haematuria; subacute—albuminuria; chronic—ureæmia.

Congenital Polycystic Disease of the Lungs.

DR. D. M. GEPP presented a girl, aged two years and one month, who had been first examined at the Children's Hospital one year previously. She had a past history of measles at the age of ten months, and clinically resembled a sufferer from pink disease, exhibiting symptoms of irritability, insomnia, anorexia and loss of weight. On examination, she resented being handled; her tonsils were found to be enlarged and inflamed, but examination of her chest revealed only an odd rhonchus. She was treated with penicillin and a course of sulphamezathine, but the signs in her chest increased, being those of bronchitis when she was examined one month later. Her cough increased and became progressively looser, and X-ray examination showed patchy consolidation in the lower zone of the left lung. She was admitted to hospital for investigation and treatment. After a further course of penicillin her chest cleared somewhat, and X-ray examination at this stage revealed a diffuse bilateral, polycystic condition of the lungs, most marked at the base of the left lung. This was confirmed by bronchoscopy and bronchogram. No similar polycystic condition of the kidneys was shown by X-ray examination. In view of the extent of the condition, surgical treatment was not considered possible. Dr. Gepp went on to say that the course of the patient's condition over the past six months had been one of recurrent chest infections with constant productive cough. Culture of sputum produced a profuse growth of *Proteus vulgaris*, resistant to streptomycin, aureomycin and "Chloromycetin", and a scanty growth of *Staphylococcus aureus*, sensitive to aureomycin and "Chloromycetin". In view of the claim that "Gantrisin", a new sulphonamide, had some effect in controlling *Proteus* infections, the patient was given a maintenance dose of this drug. It was of interest that in the most recent sputum culture only *S. aureus* was grown.

Pyogenic Meningitis.

DR. D. A. McCREDIE presented three patients who had been suffering from pyogenic meningitis to illustrate the treatment of the condition at the Children's Hospital.

The first patient, a boy, aged five and a half years, had presented with a history of recurrent discharging left ear for eleven days, for which he had been given chloramphenicol. In the last twenty-four hours his condition had deteriorated; he had severe headache and was vomiting. On examination of the child, his temperature was 105·6° F., he had gross neck stiffness, and he was irritable and disorientated. Thick yellow pus was seen in the left ear. General examination revealed no abnormality. Lumbar puncture produced turbid fluid with approximately 4000 cells per cubic millimetre, mostly polymorphonuclear cells. No organisms were seen on examination of a Gram-stained smear, but culture of both cerebro-spinal fluid and material from an aural swab produced β haemolytic streptococci, which were penicillin-sensitive. Treatment was with intrathecal penicillin administration, 20,000 units daily for five days. Intrathecal streptomycin therapy was given until the culture report was obtained. Penicillin, 100,000 units three-hourly, and sulphadimidine, one gramme four-hourly, were given for ten days. After eight days the child's temperature was completely normal, he was clinically very well, and his ear drum had healed. He remained very well, and his cerebro-spinal fluid appeared normal three days after treatment had been discontinued. One month later, he appeared a normal little boy in every way.

The second patient, a boy, aged one year and nine months, had presented with a history of being rather languid and vomiting on the day of admission to hospital; he had an attack of convulsions a quarter of an hour before admission. On examination, he was found to be a cyanosed baby in convulsions with a temperature of 104·2° F., neck stiffness and increased jerks on the left side. His throat was redened. General examination revealed no abnormality. Lumbar puncture produced a turbid fluid containing 2700 polymorphonuclear cells per cubic millimetre; on culture of the fluid *Hæmophilus influenzae* type B was grown. Treatment was with intrathecal administration of streptomycin, 30 milligrammes twice daily for five doses, and then daily for three more (six days all told); by then his general condition was considerably improved, and he was walking around the cot. Intramuscular administration of streptomycin, 175 milligrammes six-hourly, and of sulphadimidine, one gramme six-hourly, was continued for nine days; by then he seemed completely normal. Lumbar puncture four days after chemotherapy had been discontinued yielded normal findings. He was discharged from hospital to his

home on the fourteenth day and again appeared a normal little boy.

The third patient was a girl, aged one year and seven months, who had presented three weeks previously with a five-days history of feverishness and listlessness. On examination, she was found to be a very pale listless baby with a temperature of 104·4° F. and pronounced neck stiffness. Her left ear drum was inflamed. Lumbar puncture produced opalescent fluid containing 850 polymorphonuclear cells per cubic millimetre, and on culture *Streptococcus pneumoniae* was grown. The haemoglobin value was 60%. Penicillin, 20,000 units daily, was given intrathecally for five days; then penicillin, 100,000 units three-hourly, and sulphadimidine, one gramme six-hourly, were given for one week, and penicillin, 100,000 units three hourly, for eleven days. A blood transfusion of eight ounces was given. The child's condition improved rapidly, and the cerebro-spinal fluid was normal three days after treatment had been discontinued. The patient now appeared perfectly normal.

Dr. McCredie pointed out that in all cases, full chemotherapy, with penicillin and streptomycin given both intrathecally and intramuscularly, and sulphadimidine given intramuscularly or orally, was carried on until a culture report was obtained.

Coarctation of the Aorta.

DR. M. L. POWELL presented a series of three patients suffering from coarctation of the aorta, all strikingly similar in most points but showing differences in angiographic appearances. The patients' ages were three years (a boy), four years (a girl) and nine years (a boy). All were symptomless, though the boy of nine years was very much underweight. All had a systolic bruit, maximal to the left of the sternum, well up under the clavicle and audible posteriorly. Pulsating vessels around the scapula were present only in the boy of nine years; the *dorsalis pedis* vessels were palpable in all three. Blood pressures were not elevated except possibly that of the boy of nine years, who had a systolic pressure of 135 millimetres of mercury and a diastolic pressure of 80 millimetres in both arms. Angiography demonstrated in the boy of three years and in the girl of four years an identical lesion—namely, a curiously tortuous kinked and narrowed transverse arch of the aorta, the kink being greatest at the ductus site. The lesion appeared to be a grade of coarctation, but it was probably not operable owing to the length of aorta involved. The boy of nine years had a classical "adult" type of coarctation, which would be eminently operable should the need arise.

Paroxysmal Tachycardia.

Dr. Powell also presented a baby, aged ten months, who had been admitted to the Children's Hospital in June and again, in July, 1951, with extremely severe bronchopneumonia and a considerable amount of bronchial spasm (there was a strong family history of asthma). On the child's second admission to hospital a systolic bruit had been heard, the cardiac rate was extremely rapid even when the baby was afebrile, and the heart shadow in the X-ray film was obviously enlarged, though of normal contour. An electrocardiogram showed auricular paroxysmal tachycardia. The method of management of the baby since had been to endeavour to control the abnormal rhythm with digitalis. As the result of administration of "Digitoxin", 0·1 milligramme three times a day for forty-eight hours, followed by 0·05 milligramme six-hourly, normal rhythm had been restored for short periods only, a slight and doubtful decrease had occurred in the cardiac outline in X-ray films, and the systolic bruit was barely audible. Throughout the weeks of trial of digitalis the baby had been perfectly happy and seemed strikingly undistressed by the rapid cardiac action. Dr. Powell said that the diagnosis might be auricular septal defect with paroxysmal tachycardia, or possibly the disturbance of rhythm was the sole abnormality; the cardiac dilatation and systolic bruit might be secondary phenomena, which might vanish if the rate could be controlled.

Valvular Pulmonary Stenosis.

Two post-mortem specimens were shown. The first was a perfect example of valvular pulmonary stenosis with auricular septal defect—essentially an operable lesion. The second was a curious case of valvular pulmonary stenosis in a baby who had died after four days. Dr. Powell pointed out that the stenosis was not the usual truncated cone type of valve, but was produced by a small mass of tissue suspended, as it were, by "guys" from the periphery of the vessel, the whole effect being to produce a very effective block in the lumen. One strange effect of this was that the murmur produced was not the typical harsh pulmonary

stenotic bruit, but a distinctly continuous bruit which was exactly like a ductus bruit, but was obliterated by crying. Apparently the crying so raised the pulmonary pressure that very little blood was able to get through the stenotic area and the bruit ceased. Dr. Powell stated that it was the first time he had heard a continuous bruit produced in that manner.

Congenital Heart Disease

DR. H. HILLER showed three patients with congenital heart disease and a number of angiocardiograms from cases of Fallot's tetralogy and pulmonary stenosis.

The first patient was a boy of eight years who had been diagnosed as suffering from Fallot's tetralogy with a patent *ductus arteriosus*. All the clinical findings of Fallot's tetralogy were present, and the diagnosis had been confirmed by angiocardiology. However, the boy had a typical machinery murmur, maximal behind the sternum and therefore further to the right than was usual. The diagnosis rested between a patent ductus and enlarged collateral lung vessels. It was felt that the former was the more likely diagnosis, as the murmur had been known to be present since a few months after birth. The angiogram did not show a definite ductus abnormality, but it did explain the unusual position of the continuous murmur, as the aorta was shown to be completely right-sided. The question of possible operation was raised during discussion, but it was pointed out that the boy had had what amounted to a physiological operation already, and the risk of strain on the right side of the heart would be very great if any shunt operation was performed.

Dr. Hiller's second patient was a boy of nine years who was symptomless. The interest in the case was the fact that clinically the boy could be regarded as having a mild grade of auricular septal defect, whereas all investigations pointed to a mild degree of pure pulmonary stenosis. Clinically there was evidence of right ventricular hypertrophy with a wide splitting of the pulmonary second sound and a harsh systolic murmur maximal at the pulmonary area. However, although the evidence pointed towards an auricular septal defect, and although the electrocardiogram showed a right axis deviation and right ventricular hypertrophy with very early right bundle branch block leads in V_1 and V_2 , the X-ray films revealed clear lung fields, and the angiocardioogram revealed a grossly dilated pulmonary artery with a mild grade of valvular stenosis and no evidence of septal defect.

Dr. Hiller finally presented a girl of six years with typical aortic stenosis of congenital origin. She was clinically very well, and her findings were classical for the condition. Dr. Hiller explained that he particularly wished to demonstrate the typical post-stenotic dilatation of the aorta which occurred in such cases, and which could be very prettily shown by angiography. As was usual in such cases, it was impossible to demonstrate the actual stenosis.

Precocious Sexual Development.

DR. L. P. WAIT presented three patients who demonstrated different types of precocious sexual development. A girl, now aged five years, had first attended the hospital when aged one year and nine months with a history of vaginal bleeding one month prior to the visit and again just two days before the visit. Her mother had also noticed that her breasts had developed. She appeared to have developed more rapidly both physically and mentally than her brother, who was two years older. Examination of the child at that time revealed a well-developed girl who was big for her age. Vaginal bleeding was noted. The breasts were well developed and proportionate to her size. The external genitalia were well developed, and there were some fine pubic hairs. Another apparent feature was her modesty. No other abnormality was detected. Dr. H. F. Bettinger, of the pathology department of the Women's Hospital, Melbourne, examined vaginal scrapings and gave the following opinion: "The pattern of the scrapings corresponds very closely to that seen in an adult woman at the height of the follicular phase just before ovulation. It indicates marked oestrogenic activity." X-ray examination of the long bones revealed advanced ossification of the epiphyses. X-ray examination of the skull revealed no abnormality. Dr. J. G. Whitaker performed a laparotomy. The uterus, Fallopian tubes and ovaries were developed to the size seen in a normal adult female. No tumour of the ovary was discovered. Dr. Wait said that since her first attendance the child had menstruated regularly every twenty-eight days. She now showed all the signs of normal puberty. She was extremely modest and sensitive. Her precocious sexual development was probably due to normal constitutional causes which had developed prematurely.

The second patient presented an example of virilism due to a suprarenal tumour. She had first attended the hospital at the age of six years, when she had pronounced over-development of the external genitalia with a good growth of black pubic hairs. There were also some axillary hairs. There was no breast development, and there had been no vaginal bleeding. She was a dull apathetic child and looked like a "little old woman". An X-ray examination of the abdomen revealed a large calcified tumour situated above the right kidney, this being vividly portrayed in the X-ray film after peritoneal insufflation of air. The urinary androgen (17-ketosteroid) content was 15 milligrammes in a twenty-four hours specimen of urine (the normal value for a child aged five to six years was four milligrammes). Dr. John Begg operated on the girl and removed a large tumour of the right suprarenal gland; it was about the size of an orange. Her convalescence was uneventful. Dr. Reginald Webster examined the tumour and gave the following report:

Microscopy showed excessive vascularity with much necrosis and calcium "sand". Although there are fields in which the zona fasciculata of the adrenal is preserved, there are many aberrant cells, many of which show mitoses. The difficulty in microscopic diagnosis is the interpretation of the aberrant cells as between malignant metaplasia and degenerative change.

That was six years ago. The girl was still alive and well. There was no clinical or radiological evidence of recurrence. After operation the girl's development underwent a dramatic change. She became an active, bright girl, and her school work improved. The pubic hairs, though reduced in number, did not completely disappear. The results of follow-up estimations of 17-ketosteroids were 1.4 milligrammes in 1946, 0.9 milligramme in 1948 and one milligramme in 1951. Menstruation commenced in 1951 when the child was aged thirteen years. Examination showed that she was developing the normal female characteristics associated with puberty.

The third patient presented an example of precocious puberty, due to an ovarian tumour. She had been referred to Dr. Wait by Dr. David Pitt. The child was aged eleven months, and the mother had noticed increasing distension of the abdomen and enlargement of the breasts for the past two to three months. The child was quite well otherwise. There had been no vaginal bleeding. Examination of the child revealed gross abdominal enlargement and well-developed breasts. The external genitalia were over-developed for her age, and there were some fine and coarse pubic hairs. Examination under general anaesthesia revealed a large mobile abdominal tumour.

Dr. J. G. Whitaker operated on the girl and removed a large tumour of the right ovary, the longest "diameter" being ten inches. The uterus was abnormally large for a child. On the third day after operation vaginal bleeding occurred. That was regarded as an oestrogen-withdrawal effect. Dr. H. F. Bettinger, of the Women's Hospital pathology department, examined vaginal scrapings and gave the following report:

There is a preponderance of cornified cells and is comparable with those obtained from a woman at the height of the follicular phase. This represents a marked estrogenic effect.

Section of the tumour showed numerous large and small cysts with very little solid tissue. Microscopic examination showed cystic spaces lined by cuboidal epithelium. Granulosa cells were not seen. Dr. Wait pointed out that on the night of presentation of the child at the meeting a month had elapsed since operation. The striking point about the child's appearance now was the considerable decrease in the size of the breasts. The external genitalia were also assuming normal size.

Photographs of the patients and specimens, prepared by Mr. Murphy, of the hospital photographic department, were demonstrated together with the patients.

Foreign Body in the œsophagus.

Dr. Wait related the history of a child, aged two years, who had suffered from an unusual foreign body which had become impacted in his oesophagus. While eating an egg he had suddenly cried with pain in his chest and vomited several times. The pain subsided with rest. For the next six days he suffered a recurrence of the pain whenever he ate solid food, but it did not occur with liquids and soft foods. He was very hungry and desired solid food. Dr. Wait first examined him on the sixth day and diagnosed a probable foreign body in the oesophagus. An X-ray examination of the chest revealed a crescentic shadow about one

inch in length in the line of the oesophagus about the level of the tracheal bifurcation. Dr. Raymond Hennessy removed a large piece of egg shell via the oesophagoscope. Convalescence was uneventful, and symptoms were relieved.

Antibiotics in Acute Infections.

DR. STANLEY WILLIAMS demonstrated the use of antibiotics in acute infections and showed that penicillin was still the most important single antibiotic. He said that the use of oral penicillin therapy was not generally appreciated, although its administration by that route should not be practised in severe infections. Staphylococcal infections were found more frequently than hitherto to be due to penicillin-resistant organisms and aureomycin was the antibiotic of choice in such instances. It could be combined with penicillin when there was doubt as to the ideal antibiotic for a particular infection. It was unwise to give "Chloromycetin" and penicillin together, for there was some indication that "Chloromycetin" neutralized to a degree the effect of the penicillin. "Chloromycetin" had been most disappointing in the treatment of whooping-cough. In a series of patients treated with terramycin, Dr. Stanley Williams showed that terramycin was an effective form of treatment in cases of pneumococcal pneumonia, acute tonsillitis and *Bacillus coli* urinary tract infection. He said that there were still a number of respiratory and other infections which clinically did not respond to any antibiotic; as an example of that, the X-ray films were shown of a boy, aged seven years, who had died from bronchopneumonia in spite of chemotherapy and the use of the most modern antibiotics.

Vomiting in a Newborn Child.

DR. V. L. COLLINS presented a demonstration relating to vomiting in a newborn child in the first few weeks of life.

Dermatological Conditions.

DR. ARTHUR J. DAY showed patients to demonstrate the results of treatment of haemangioma with carbon dioxide snow, X rays and radium. He advocated the use of snow only for lesions raised three millimetres or less above the surface. He said that the earlier such patients were treated the greater the chance of good results from the use of simple methods, particularly if irradiation was necessary, as the younger the lesion the greater the relative radiosensitivity. However, after the age of two and a half years the relative sensitivity was lost, and then surgery was probably the treatment of election.

Dr. Day also demonstrated a series of patients suffering from infantile eczema and flexural dermatitis, showing the change in distribution of the rash from the extensor surfaces to the flexures when the child became old enough to appreciate the pleasurable sensation of rubbing the flexures, and explained the differences in treatment advisable.

DR. F. BAUER demonstrated the use of ultra-violet light in the diagnosis and treatment of *tinea capitis* and showed the necessity for cutting the hair short over the whole scalp while treatment was being carried on.

Erythroblastosis Foetalis.

DR. ELIZABETH TURNER gave a brief résumé of the Rh factor. She indicated how iso-immunization of the mother might occur in a heterospecific pregnancy, and described the varying degrees of hemolytic disease in a fetus from such a pregnancy. Dr. Turner's demonstration dealt chiefly with the management and treatment in such cases. She said that the possible methods of treatment could be classified under two headings.

Under the heading of prophylactic treatment the following methods could be classified: (i) To prevent mating between an Rh-negative woman and an Rh-positive man. (ii) To discover a method to render the woman incapable of producing antibodies. (Methods (i) and (ii) were still in the realm of impracticability.) (iii) To absorb any antibody formed by the use of Rh hapten, a method which had been acclaimed by Bettina Carter. (iv) To prevent transference of antibodies across the placental barrier. B. S. Ten Berge, of the University of Groningen, had reported success by the use of α -tocopherol given by mouth to the mother during her pregnancy. His results did not seem to be substantiated by results from a clinical trial at present being undertaken at the Queen Victoria Memorial Hospital, Melbourne. (v) To prevent cerebral damage in the infant (which had been considered by Philipott, of England, to be secondary to liver damage) by the administration of methionine to the mother during pregnancy. The reported results had not been substantiated in Melbourne. (vi) To induce labour before the

antibody titre rose to a dangerous level. Dr. Turner considered that induction of labour after the thirty-seventh week of gestation was fraught with little risk to the infant, and might prevent intrauterine death in cases in which the antibody titre rose rapidly in the last few weeks. (vii) To protect the infant passively against the effects of antigen-antibody reaction, by giving of ACTH during the first few days of life. ACTH had been reported to be effective in the prevention of hemolytic disease in the infant in the United States of America; and in Melbourne a clinical trial at present being undertaken showed indications of promise.

The second heading was actual treatment of the haemolytic manifestations, and under it the following methods could be grouped: (i) By simple transfusions of Rh-negative blood when the infant's blood hemoglobin percentage fell below 75 in the first two weeks of life, 60 during the second two weeks and 50 during the third two weeks. (ii) By replacement, or exchange transfusion, which was the only method of removing large amounts of antibody from the infant's circulation, and of removing haemoglobin, the precursor of bilirubin. Dr. Turner considered such a transfusion to be also an effective method in the correction of anaemia. The indications for replacement transfusion were: primarily, a poor obstetric past history, with previously affected infants; secondly, a cord blood haemoglobin value of less than 100%; thirdly, a strongly positive direct result from a Coombs test on the cord blood; fourthly, a cord serum bilirubin content greater than seven milligrams per 100 millilitres.

Dr. Turner then demonstrated on a working model a simple method of replacement transfusion in which a three-way tap was used. One way was connected to a flask containing citrated Rh-negative donor blood, with a haemoglobin content corrected to 15 grammes per centum. The second way was attached to "Polythene" tubing of 2.5 millimetre diameter, which was passed into the umbilical vein through the cut end of the cord and served as the route for removal and giving of blood. The third way led into a waste collecting and measuring bottle, with a small side tap connected to a bottle of heparinized saline, which could be used to flush the apparatus should clotting occur. The three-way tap was connected to a metal and glass syringe, and the blood was replaced in ten millilitre lots. Dr. Turner said that no trouble had been experienced with replacements commenced on infants whose ages ranged from four to twelve hours. She aimed at replacing 80 millilitres per pound of body weight, in an average time of one and a half to two hours. The desired haemoglobin value at the end of transfusion was 120% if the baby's condition was satisfactory. It had not been found necessary to give calcium gluconate to combat the effects of the citrate. Antibiotics, such as penicillin, were given to the infants as a routine after replacement transfusion. As the duration of the hemolytic process had been found to continue over the first fifty or sometimes sixty days of life, it was imperative to have adequate follow-up of the infants, with daily and later weekly estimations of the haemoglobin content of the blood.

Dut of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

GOVERNOR MACQUARIE TO LORD BATHURST.¹

Government House,
Sydney,
November 9, 1820.

My Lord,

I have the honour to acknowledge the receipt of your Lordships letter no. 9 dated the 10th of July 1820 relative to the King's disapproval of my appointing Mr William Redfern, late assistant Surgeon in the Medical Staff of this Colony, a magistrate, and directing him to be removed from that office. I have now to report to your Lordship that the King's Commands have been carried into effect in respect of the removal of that gentleman from the office of Magistrate.

I have, &c.,
L. MACQUARIE.

¹ From the original in the Mitchell Library, Sydney.

Post-Graduate Work.

THE MELBOURNE PERMANENT POST-GRADUATE COMMITTEE.

PROGRAMME FOR MAY, 1952.

Course Suitable for Candidates for M.D. Part II and M.R.A.C.P.

A COURSE on endocrinology, under the direction of Dr. K. D. Fairley, will be held at 2 p.m. on the following dates: May 13: Dr. J. H. Bolton, at the Royal Melbourne Hospital, "Diseases of the Pituitary Gland". May 16: Dr. E. Downie, at the Alfred Hospital, "Carbohydrate Metabolism in Relation to the Endocrines". May 20: Dr. K. D. Fairley, at the Royal Melbourne Hospital, "Diseases of the Thyroid Gland". May 20: Dr. R. M. Biggins, at Saint Vincent's Hospital, "Diseases of the Parathyroid Glands". May 27: Dr. J. W. Johnstone, at the Women's Hospital, "The Endocrinology of the Female". May 30: Dr. R. Andrew, at the Alfred Hospital, "Diseases of the Adrenal Glands".

The fee for this course is £3 3s., or 10s. 6d. per lecture.

Country Courses.

Port Fairy.

A post-graduate lecture will be held in the Borough Chambers, Port Fairy, on May 3, at 8 p.m. Dr. R. M. Biggins will speak on "Cortisone and ACTH Adaptation Syndrome". Enrolments should be made with Dr. W. R. Angus, Honorary Secretary of the South-West Subdivision of the British Medical Association, 214 Kororoit Street, Warrnambool. Telephone 52. The fee will be 10s. 6d.

Bendigo.

A post-graduate course will be held at Lister House, the Northern District School of Nursing, Rowan Street, Bendigo, on May 10 with the following programme: 2.15 p.m., Dr. J. B. Somerset, "Haematuria"; 4.15 p.m., Dr. B. Keon-Cohen,

"Low Back Pain"; 8.15 p.m., Dr. Leslie Hurley, "Medical Emergencies". Enrolments should be made with Dr. Warwick Rosenthal, Honorary Secretary, Bendigo Subdivision of the British Medical Association, 32 View Street, Bendigo. Telephone 477. The fee will be £1 1s. 6d. for the course, or 10s. 6d. per demonstration.

Flinders Naval Depot.

A demonstration will be conducted by Dr. K. Newman Morris on "Treatment of Bronchiectasis" at Flinders Naval Depot on May 14 at 2.30 p.m. This is by arrangement with the Royal Australian Navy.

Course for D.D.R. Part II.

It has been decided to hold a course for candidates for the D.D.R. Part II commencing about the middle of July, 1952. This course will involve a series of lectures and demonstrations in radiodiagnosis, and also a short course in special pathology.

Courses for Part I of Higher Degrees and Diplomas.

Courses for candidates for Part I of higher degrees and diplomas will be continued during May with certain intervals during the university vacation period.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Diploma Courses: Clinical Pathology, Psychological Medicine Part II, Dermatological Medicine Part I.

The Post-Graduate Committee in Medicine in the University of Sydney will hold a course for candidates for the diploma in clinical pathology, commencing in July, 1952, provided a sufficient number of candidates is offering.

The committee will conduct a course for candidates for Part II of the diploma in psychological medicine, commencing in May, 1952.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED MARCH 8, 1952.¹

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism
Anæstomiasis	2	2
Ancylostomiasis
Anthrax
Bilharziasis
Brucellosis	1	1
Cholera
Chorea (St. Vitus)
Dengue
Diarrhoea (Infantile)	5(2)	8(2)	2(2)	..	2(1)	..	2	..	4
Diphtheria ..	6(6)	14(13)	17
Dysentery (Bacillary)	20
Encephalitis
Filariasis
Homologous Serum Jaundice
Hydatid
Infective Hepatitis	1	12(9)	..	2	..	1
Lead Poisoning	1	1
Leprosy	1
Leptospirosis
Malaria
Meningococcal Infection ..	3(3)	4(2)	1	..	1	..	1	..	10
Ophthalmia
Ornithosis
Paratyphoid	1	1
Plague
Pollomyelitis ..	2(1)	7(2)	3(1)	22(16)	2(1)	36
Puerperal Fever
Rubella	1	1	2
Salmonella Infection
Scarlet Fever ..	9(2)	32(20)	1	1(1)	4(4)	1	..	1	49
Smallpox
Tetanus	2	1	3
Trachoma
Trichinosis
Tuberculosis ..	19(18)	18(8)	19(14)	12(7)	9(5)	7(3)	3	..	82
Typhoid Fever	1	1
Typhus (Flea-, Mite- and Tick-borne)	1	1
Typhus (Louse-borne)
Yellow Fever

¹ Figures in parentheses are those for the metropolitan area.

Physiology lectures in the Part I course for candidates for the diploma in dermatological medicine will begin early in May, 1952, provided a sufficient number of candidates is offering.

Candidates intending to take part in these courses are asked to communicate as soon as possible with the Course Secretary, the Post-Graduate Committee in Medicine, 131 Macquarie Street, Sydney.

Lecture on Modern Methods in the Use of Penicillin.

Dr. D. K. Kitchen, M.D., Chief Medical Counsel of Bristol Laboratories, Incorporated, New York, will speak on "Modern Methods in the Use of Penicillin" on Friday, April 4, 1952, at 8 p.m., in the Stawell Hall, 145 Macquarie Street, Sydney. The lecture will deal with the single treatment schedules, the placental transfer of penicillin, and single injection studies in syphilis and other diseases, with special reference to blood levels. The lecture has been arranged for members of the annual subscription course.

Obituary.

MAGNUS JOHN MAY.

We regret to announce the death of Dr. Magnus John May, which occurred on March 11, 1952, at Brighton, Victoria.

MYLLES WYAMARUS CAVE.

We regret to announce the death of Dr. Myles Wyamarus Cave, which occurred on March 17, 1952, at Beeac, Victoria.

VIVIAN JOSEPH MANKEY.

We regret to announce the death of Dr. Vivian Joseph Mankey, which occurred on March 18, 1952, at East Malvern, Victoria.

THOMAS NATAL BOLGER.

We regret to announce the death of Dr. Thomas Natal Bolger, which occurred on March 23, 1952, at Sydney, New South Wales.

WILLIAM SYDNEY GLEESON.

We regret to announce the death of Dr. William Sydney Gleeson, which occurred on March 26, 1952, at Sydney, New South Wales.

Honours.

Major (Temporary Brigadier) Charles Wason Nye, E.D., has been created by His late Majesty King George VI an Officer of the Military Division of the Most Excellent Order of the British Empire, for outstanding non-operational services.

Australian Medical Board Proceedings.

NEW SOUTH WALES.

The following have been registered, pursuant to the provisions of the *Medical Practitioners Act*, 1938-1950, as duly qualified medical practitioners: Brandwein, Aniela Teresa, registered in accordance with the provisions of Section 17 (1) (c); McLachlan, Hugh Kenneth Ian, M.B., B.S., 1951 (Univ. Melbourne); Petrovsky, Constantine Constantinovich, M.B., B.S., 1938 (Univ. Hong Kong); Straede, William Thomas Charles, M.B., B.S., 1950 (Univ. Melbourne); Wall, Thomas Charles, M.R.C.S. (England), L.R.C.P. (London), 1951.

The following additional qualification has been registered: Nevell, Thomas Franklin (M.B., 1946, Univ. Sydney), B.S., 1949 (Univ. Sydney).

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Hurt, Bruce Raymond Mostyn, M.B., B.S., 1948 (Univ. Sydney), Sydney Hospital, Sydney.

Costello, William Thomas, M.B., B.S., 1951 (Univ. Sydney), Royal Prince Alfred Hospital, Camperdown.

The undermentioned has applied for election as a member of the Victorian Branch of the British Medical Association:

Wall, Thomas Charles, L.R.C.P. (London), M.R.C.S. (England), 1951, 30 Raglan Street, Sale.

Diary for the Month.

APRIL 8.—New South Wales Branch, B.M.A.: Executive and Finance Committee.

APRIL 8.—New South Wales Branch, B.M.A.: Organization and Science Committee.

APRIL 14.—Victorian Branch, B.M.A.: Finance Subcommittee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 226 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in the Commonwealth can become subscribers to the journal by applying to the Manager or through the usual agents and book-sellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £5 per annum within Australia and the British Commonwealth of Nations, and £6 10s. per annum within America and foreign countries, payable in advance.

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